

# Bactrim DS

Each tablet contains 160 mg trimethoprim and 800 mg sulfamethoxazole.

## double strength tablets

### Just 1 tablet b.i.d. for better patient compliance

For chronic or frequently recurrent urinary tract infection.



**Just 1 tablet b.i.d.**

When the patient with chronic or frequently recurrent urinary tract infection fails to comply with therapy, persistent bacteriuria or relapse may occur. Single tablet b.i.d. dosage makes compliance easier.

**Same efficacy with half the number of tablets**

Studies have established bio-equivalency of Bactrim DS double strength tablets with the Bactrim single strength tablets.

**Greater economy for patients**

Fewer tablets per day offer sufficient medication for the full course of therapy at a lower cost to the patient.

Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis, or pyelitis due to susceptible strains of *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris* and *Proteus morganii*.

**NOTE:** The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method (Federal Register, 37:20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Bactrim therapy. If infection is confined to the urine, "Intermediate susceptibility" also indicates a likely response. "Resistant" indicates that response is unlikely.

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

**Warnings:** Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hemopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. Data are insufficient to recommend use in infants and children under 12.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid

intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, anemia, purpura, thrombopenia, leukopenia, hemolytic anemia, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, anorexia, abdominal pains, hepatitis, diarrhea and pancreatitis. **CNS reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarthritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diabetes and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

**Dosage:** Not recommended for children under 12. Usual adult dosage: 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen.
15-30	1 DS tablet (double strength) or 2 tablets (single strength) or 4 teasp. (20 ml) every 24 hours
Below 15	Use not recommended

**Supplied:** Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100; Tel-E-Dose® packages of 100. Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40, available singly and in trays of 10. Oral suspension, containing in each teaspoonful (5 ml) the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole; fruit-licorice flavored—bottles of 16 oz (1 pint).

## Bactrim DS

double strength tablets  
(160 mg trimethoprim and 800 mg sulfamethoxazole)

For chronic cystitis and pyelonephritis evidenced by persistent bacteriuria and due to susceptible organisms

ROCHE  
Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

# Medical Tribune

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and Medical News

Vol. 17, No. 23

world news of medicine and its practice—fast, accurate, complete

Wednesday, July 7, 1976

## MD Countersues, Wins: It's a New Ballgame



Alarms in Chicago malpractice tangle were x-rays taken by Dr. Leonard Berlin (above) showing dislocation of little finger (bottom views). Reduction films (top) later revealed chip fracture at base of involved joint. Patient sued, but radiologist countersued, contending fracture was not visible initially and that treatment was same in any case. See page 4.

## Dr. Davis Regrets 'Negative Effects'

### Med School Minority Program Rap Sparks Indignation & Rue

By MICHAEL HERRING  
Medical Tribune Staff

**Boston**—An article in the *New England Journal of Medicine* linking a decline in medical school academic standards with the practice of graduating some minority students "on a charitable basis" has inflamed indignation among academic communities and the media to such a point that the author, Dr. Richard Davis of Harvard Medical School, has publicly apologized.

Dr. Davis, who is Adele Lehman Professor of Bacterial Physiology, told *Medical Tribune* that the apology, printed in the *New York Times* and *Harvard Gazette*, was issued "to try to neu-

tralize the negative effects in the public image and the morale of minority medical students" caused by the furor. The worst of these negative effects, he said, has been the rejection of a few young black doctors by patients who saw excerpts of his remarks in the lay press.

However, Dr. F. Sargent Cheever, Harvard's Director of Admissions, told *MEDICAL TRIBUNE* that Dr. Davis is an "idealist, not a racist, who has worked for minorities," and that there is indeed a danger of "letting our hearts run away" in trying to rectify social injustice, if degrees are granted to minority-group students at the expense of

Continued on page 22

## Resolves Ascites, Bleeding

### Anti-Gout Drug Proves Effective In Cirrhosis

By NATHAN HORWITZ  
Medical Tribune Staff

**MIAMI BEACH**—Colchicine, conventionally prescribed for gout, is proving effective in the treatment of cirrhosis, a Mexican team has reported.

A double-blind trial of the drug in patients with severe cirrhosis resulted in the resolution of ascites and edema and an end of bleeding episodes in treated subjects, compared with "no clinical improvement" in the placebo group, the American Association for the Study of Liver Diseases was told here.

Some 40 additional patients who have been added to the study since the

Continued on page 15

## Concern, Yes, But

### 'Over-Reaction' to Estrogen-Ca Link Seen Detrimental

Medical Tribune World Service

**VANCOUVER, B.C.**—There has been an "over-reaction" to the news that estrogen replacement may increase the risk of endometrial cancer, the President of the American Radium Society (now Oncology Society of America) said here. Speaking at the society's 58th annual

Continued on page 9

## Ultrasound Visualizes Deep Pelvic Organs



Stage C carcinoma of the bladder (T) is shown through use of new ultrasonic technique that visualizes bladder, prostate for first time. See page 29.

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Sheaffer Pen (UK)  
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Somerville Stores  
Sony United King  
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## INTERNATIONAL REPORT

from Japan from the Editors of Medical Tribune Japan, Tokyo

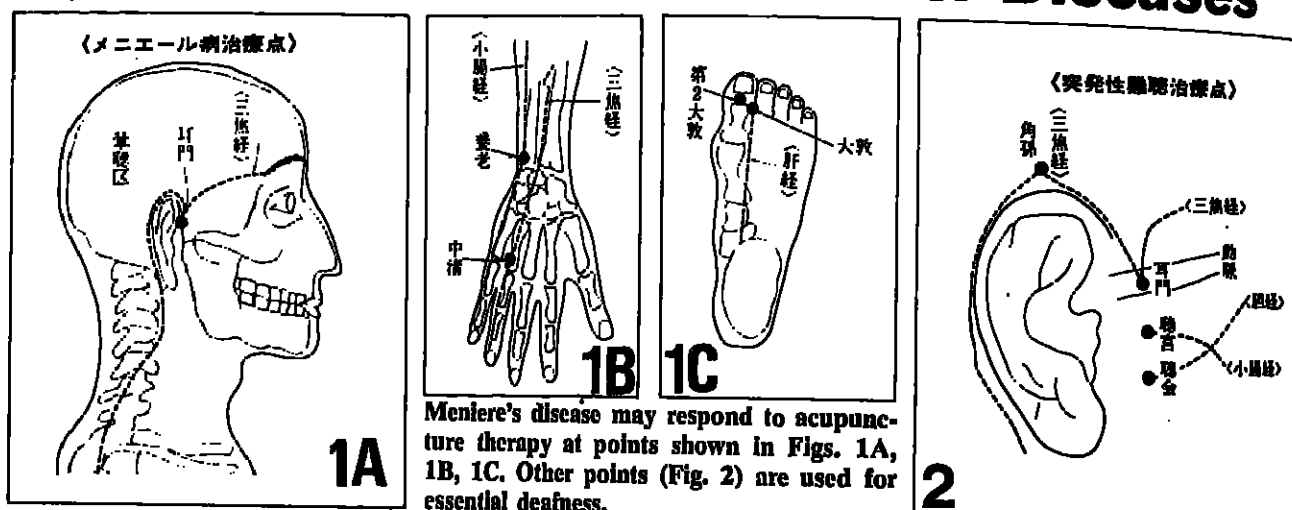
## Acupuncture May Relieve Meniere's and Other Diseases

Medical Tribune World Service

TOKYO—Although acupuncture therapy has been found to be of limited value in a pain clinic, it appears to relieve some symptoms in intractable forms of Meniere's disease, essential deafness, Bechet's disease, Sjögren's disease, and subacute myeloneuropathy (SMON). Dr. Kumio Yamashita, anesthesiologist at the National Hospital Medical Center here, reported at a meeting of the Tokyo Health Insurance Physicians Association.

In response to a government call for therapeutic programs for diseases which it has officially designated as intractable.

Continued on page 23



Meniere's disease may respond to acupuncture therapy at points shown in Figs. 1A, 1B, 1C. Other points (Fig. 2) are used for essential deafness.

from Britain from the Editors of Medical News-Tribune, London

## English GPs Work Very Differently from Iowa Colleagues

By DR. VIVIEN CHOO  
Medical Tribune World Service

STRAFORD-UPON-AVON—GPs in north-east England evidently work very differently from GPs in Iowa. For a start, English GPs do not examine one in

eight of their patients. In Iowa, history taking is minimal, but GPs there carry out full examinations on about half their patients—three times as often as do English GPs.

In addition, American GPs take the

temperatures of five times as many patients, use their stethoscopes on twice as many, record the blood pressures of four times as many and examine the fundi of 10 times as many patients, as do English doctors.

Yet the average length of consultation in Iowa is not much longer than in England.

These findings come from a survey in which 25 GPs in NE England and

Continued on page 23

from Germany from the Editors of Medical Tribune Germany, Wiesbaden

## Animal Contact May Play Decisive Role in Hodgkin's Disease

Medical Tribune World Service

HAMBURG—Epidemiological follow-up of all known cases of Hodgkin's disease in children between two and 14 years of age in North Germany since 1945 yields no support for a genetic factor or person-to-person infection, but leads rather to the conclusion that domestic animal contacts play a decisive role in the disease, reports Dr. H. Dürkin, of Hamburg-Eppendorf University Medical Clinic. In the fore-

ground are pet rabbits, followed by some other species of domestic animal. In the case of subacute sclerosing panencephalitis, there is the possibility that one might be dealing with an earlier persistent virus infection, followed by later reactivation through "complementation" or "helper virus" action. The animals are clearly symptomless carriers of the viruses and, as in other zoonotic diseases, the chain of infection comes to a full stop in man—

transmission from one person to another is very exceptional. The investigations underlying this hypothesis covered 140 children with histologically proven Hodgkin's disease, Dr. Dürkin said. Boys were affected more severely in rural areas than in the city; no urban-rural distinction was seen for girls. Mostly the disease became manifest in previously quite healthy children. Moreover, infectious mononucleosis was never encountered

in the vicinity of the children. Parents and other members of the household could be interrogated in 133 cases, yielding informative details on the environment in which the children had grown up. One-third of the parents were engaged in agriculture; three fathers were butchers and in nine other cases there were occupational contacts with animal products or feed. Nine fathers were engaged in wood processing.

Continued on page 23

from France from the Editors of Tribune Médicale, Paris

## Vague Asthenia Presents Diagnostic, Treatment Problems

Medical Tribune World Service

PARIS—General practitioners discussed their asthenic patients at a round table sponsored by the Group for the Study of Fatigue. It was led by Dr. Pierre Bugard, consulting general practitioner at the Hôpital Henri Roussel, and Dr. Louis Crocq, teaching psychiatrist in the service of Professor Pelicler at the Hôpital Necker. Following are highlights of the discussion.

Dr. Bugard pointed out that because asthenia is characterized as unclassified pathology, many physicians feel ill-equipped to deal with it. In his opinion, half the consulting patients in a general practitioner's office describe themselves as fatigued yet are actually asthenic. Dr. Bugard distinguished three groups: somatic, neurotic and reactional asthenics. Because fatigue lacks a precise definition for either doctors or laymen, a communications gap hampers physicians and their patients. A recurring statement by the panelists was that "fatigue" often screens a variety of

conflicts, personal, socio-economic, marital or sexual. The physicians agreed that, consciously or not, patients tended to "somaticize" an asthenia and that a doctor had to accept this fact. However, when Dr. Bugard asked if they considered their patients to be simulators, the response in unison was "Absolutely not."

Dr. Bugard characterized the fatigue that often serves patients' requests for leaves from work as reactional asthenia. It involves two characteristics: trauma and existential conflict. In effect, the patient demands just reparation for a situation he can no longer tolerate by seeking rest. Asthenia is a protective device, Dr. Bugard said. Its symptoms protect an individual against moral suffering resulting from anxiety. It is a fatigue that, although false, is nevertheless experienced; it must be overcome by activating the individual. The majority of doctors, agreeing with Dr. Bugard, stated that this was their first

Continued on page 23



## Bio-Marker for Alcoholism May Aid Diagnosis

By ANASTASIA TOUPEXIS  
Medical Tribune Staff

WASHINGTON, D.C.—The development of a biochemical test for alcoholism, which may eventually provide a rapid objective method for differentiating chronic alcoholics from other drinkers, is being monitored by the success of therapy.

The test, which is positive only in the presence of chronic alcohol abuse, is therefore not predictive of the development of the disease, is based on an observed characteristic alteration of plasma amino acids in alcoholics.

A significant increase in L-amino-butyric acid (AANB) relative to leucine," reported Dr. Spencer Shaw, speaking for Drs. Barry Stimmel and Charles S. Lieber. Dr. Shaw is an instructor at New York's Mt. Sinai School of Medicine and staff physician at the Bronx Veterans Administration Hospital. Dr. Stimmel is Associate Professor of Medicine at Mt. Sinai.

"This is the first time a biochemical marker for alcoholism has been reported," Dr. Lieber told MEDICAL TRIBUNE. "We have here a possible handle on the problem of alcoholism. We've never before been able to say

what makes an alcoholic different from a nonalcoholic. Here we have a biochemical difference." Dr. Lieber is Professor of Medicine and Pathology at Mt. Sinai School of Medicine and director of the Alcohol Research Laboratory of the section of Liver Disease and Nutrition at the Bronx VA Hospital. He said the test is an outgrowth of nutrition studies on baboons conducted at the Bronx laboratory.

## Hospitalized Patients

So far, the test has been evaluated in 42 hospitalized severe alcoholics and 25 methadone maintenance patients with varying degrees of alcoholism, Dr. Shaw said. Among the findings he cited:

- The ratio of AANB/leucine was significantly increased in hospitalized alcoholics compared to nonalcoholic patients.
- In the ambulatory methadone maintenance patients, the ratio increased significantly with the degree of alco-

holism as assessed by three separate standards: NCA criteria of alcoholism, a self-administered alcoholism screening test, and average daily alcohol intake. Plasma AANB/leucine was highest in patients who consumed more than 2 g/kg/day of ethanol and in patients who fulfilled major NCA criteria.

• The ratio detected most of the alcoholics identified by each of the three guidelines. In contrast, blood alcohol and liver chemistries were not useful in detecting or assessing alcoholism in the methadone group.

Dr. Shaw stressed the test is a marker for chronic alcoholism not the acute alcoholic binge.

"We hope to simplify the procedure within the foreseeable future," Drs. Lieber and Shaw told MEDICAL TRIBUNE, "so that it can be performed as a routine laboratory test." The test, which now requires an amino acid analyzer, is being used at present only on a research basis.

## Prenatal Dx of Sickle Cell Possible, But Caution Urged

By FRANCES GOODNIGHT  
Medical Tribune Staff

NEW YORK—Prenatal diagnosis of sickle cell anemia has now been achieved—but the investigators responsible for this recent and major genetic advance are sounding a cautionary note: Don't expect widespread use of the detection procedure in the immediate future.

Their reasons for the go-slow signal were outlined for MEDICAL TRIBUNE by Dr. Blanche P. Alter, of Children's Hospital Medical Center (Boston) and Harvard Medical School, who has taken part in research on prenatal diagnosis of both sickle-cell anemia and beta thalassemia.

Such studies in the United States have been largely concentrated at the Harvard complex and at the University of California, San Francisco, and the Yale-New Haven Hospital.

Dr. Alter cited difficulties posed by the procedure itself as deterrents at present to its application outside research centers.

## Fetal Blood Studied

Diagnosis of the hemoglobinopathies is made by studying hemoglobin synthesis in fetal blood (MEDICAL TRIBUNE, July 16, 1975). Red cells are identified and incubated with radioactive leucine, then the incorporation of radioactivity into beta and gamma globulin chains is measured.

Such fetal blood must be obtained by needle aspiration of the placenta or by fetoscopy, Dr. Alter pointed out. Both processes are more complicated than the amniocentesis used in detection of chromosomal or enzyme abnormalities, and fetal losses have been related to the procedures.

There is also the problem of getting sufficient blood for performance of chromatographic analyses of globulin chain synthesis, Dr. Alter said. In the 28 attempts at prenatal diagnosis of

hemoglobinopathy undertaken by the Boston and cooperating investigators, an adequate sample could not be obtained in five cases.

## Highly Complex Work

Additionally, she noted that the hemologic work is highly complex—interpretation of results was proved incorrect in two cases.

Like other investigators, Dr. Alter emphasizes that these studies are still strictly research procedures. The major area of value, in her view, will be in detecting beta thalassemia since this disorder causes death in most homozygotes by the age of 20 or earlier, and treatment in most parts of the world is unavailable or inadequate. By comparison, patients with sickle cell anemia who survive through adolescence may be able to lead fairly productive lives.

A recent report by Dr. Alter and colleagues at the Harvard complex, Yale-New Haven Hospital, and Children's Hospital of Philadelphia (New England Journal of Medicine, May 6, 1976) described the successful prenatal diagnosis of sickle cell anemia and alpha G-Philadelphia in a fetus known to be at risk because the father had both sickle cell trait and the alpha abnormality while the mother had Hb S/beta + thalassemia. The couple's only child had inherited the mother's hemoglobinopathy plus the alpha abnormality.

## Seen in 22-Week Fetus

An article in the same issue by Dr. Yuet Wai Kan and colleagues of the University of California, San Francisco, announced the detection of sickle cell anemia in a 22-week-fetus. It was the first pregnancy for the couple, both of whom were carriers of the sickle cell trait. Previously, Dr. Kan's group had reported prenatal diagnosis of beta thalassemia.

## index

CLINICAL NEWS NOTE: "After 24 months of treatment [with colchicine], all [cirrhotic] patients in the treated group were alive, without ascites and/or edema. No bleeding episodes had occurred and only one patient had encephalopathy. In contrast, no clinical improvement was seen in the placebo group and two patients died of the complications of cirrhosis. . . ." (Dr. David Kershenobich. See pp. 1, 15.)

Medicine: 1, 3, 4, 9, 15, 21, 23, 27, 29

Severe cirrhosis effectively treated by gout medication . . . 1  
Estrogen-cancer link "over-reaction" seen detrimental . . . 1  
MD apologizes for linking decline in academic standards to minority students 1  
Physician countersues patient, wins \$8,000 in damages . . . 4  
Blood pressure found high among college students . . . 4  
Histoplasmosis epidemic traced to bird droppings . . . 9  
Breast cancer: Diet being studied as explanation for variations in international incidence . . . 15  
High or low job stress both tied to disease risk . . . 21  
Unexplained retinal diseases may have interference with rhodopsin metabolism in common . . . 23  
Asthma may worsen in pregnancy . . . 27  
Ultrasonic probe visualizes prostate and bladder disorders . . . 29

## Research: 4

New drug, gemcadiol, lowers plasma cholesterol, triglycerides in lab animals. 4

## International Report: 2

## feature index

Editorial Capsules . . . 4  
In Consultation . . . 6  
Editorials . . . 11  
Letters to Tribune . . . 11  
Pediatric Progress . . . 15  
Picture Page . . . 17  
Elliott Janeway . . . 21  
Epigram . . . 27  
Medicine on Stamps . . . 27  
One Man . . . and Medicine . . . 29  
Immature Medicine . . . 29  
Medical Meeting Schedule . . . 29  
Tribune Sports Report . . . 31  
Wine Talk . . . 31

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## MD Countersues Patient, Wins \$8,000 in Damages

Medical Tribune Report

CHICAGO—Telegrams and telephone calls poured in from throughout the United States and Canada after a Circuit Court jury here awarded \$8,000 damages to a physician who had accused a patient and her attorneys of filing a frivolous malpractice suit against him.

"The reaction has been overwhelming," said Dr. Leonard Berlin, a radiologist at suburban Skokie Valley Community Hospital. "I've had calls from doctors wanting to know how to go about it and from lawyers defending doctors who want to get in touch with my lawyer."

Dr. Berlin was sued last September for \$250,000 by a 40-year-old woman who charged negligence in failing to find a small fracture in the little finger of her right hand, injured in playing tennis. The fracture was discovered in a subsequent x-ray after the patient, Mrs. Harriet Nathan, complained of continued pain.

### Treated for Fracture

In filing a counter-suit under the Illinois Barratry Act, Dr. Berlin conceded that the fracture did not show up on the first x-ray but noted that the patient was treated in the emergency room as if she had a fracture. Testimony from orthopedic witnesses confirmed the treatment as standard. Dr.

William Meltzer, who provided the treatment, also was sued but did not counter-sue.

Mrs. Nathan withdrew her suit on attorneys' advice but Dr. Berlin refused to drop his countersuit. He charged that she had "wantonly and willfully" involved him in litigation without reasonable cause. His suit also accused her lawyers, Fred Benjamin and Stuart Shapiro, of "falling below the legal standards of the community by failing to properly investigate the case." He pointed out the x-rays were available at the hospital for examination by the plaintiff's experts but that no examination was made before the suit was filed.

Dr. Berlin said he was involved in a previous malpractice suit that was settled by his insurance company without his permission "and I wasn't going to let it happen again."

He has spent \$10,000 of his own funds and 25 working days on the current case. Although asking for only \$3,000 in damages as "symbolic," the jury awarded him \$8,000 in actual and punitive damages after deliberating 15 minutes.

Several lawyers testified in support of his countersuit. Charles J. O'Laughlin, a member of one of Chicago's leading law firms, testified: "A lawyer has the duty to ascertain whether there is reason to believe the case is valid. He has a duty not to proceed if the suit will

have the effect of harassment or expense."

Wayne Giampietro, attorney for Dr. Berlin, told the jury: "This case will determine whether we attorneys are accountable in our job, just as is everyone else... Mrs. Nathan felt she was injured and somebody was going to have to pay. That is not what the law is for."

The President of the American Medical Association, Dr. Max Parrott, said the Berlin case "puts lawyers on notice that they are placing themselves in jeopardy if they do not adequately investigate a case before filing suit."

"Insurance companies estimate that it costs \$2,500 to open a claim," he continued. "These costs are borne by the doctors and, ultimately of course, by the patient."

In the view of Dr. Berlin's attorney, the verdict should have two significant spin-offs: "It means not only that an attorney must be sure there is some evidence of malpractice but also cause him to be more careful about the people he names as defendants."

Dr. Parrott said the Berlin case "is significant in part because it serves notice that doctors intend to fight back against unmeritorious cases."

Illinois has inaugurated a program designed to aid physicians willing to file counter-suits but the Berlin countersuit preceded it.

Dr. Berlin said he would like to have the jury verdict appealed up to the Illinois supreme court in order to obtain "a complete resolution of the issue." Mrs. Nathan said she intends to appeal "this grave, grave injustice."

## 'Striking Proportion' of College Students Show High BP

Medical Tribune Report

ATLANTIC CITY—A "striking proportion" of 1,671 college students in a study show elevated blood pressure, the American Federation for Clinical Research was told here.

Using the level of 130/90 to define the hypertensive threshold in young adults, investigators from the Section

of Cardiovascular Medicine at the University of California, Davis, found a significantly elevated systolic pressure in 22% of the men and 5.7% of the women, and an elevated diastolic pressure in 2.7% of the men and 0.7% of the women.

Even when 140 was considered as the upper bound of normal tension

pressure, almost 10% of the men and 2.5% of the women had readings above this level.

Additional data obtained from blood tests plus a self-administered questionnaire also indicated a strong correlation between blood pressure elevation and other factors known to pose the risk of coronary heart disease, the investigators reported.

"Since the yield of risk-factor screening was so high," they said, "it seems prudent to direct major primary preventive efforts to this age group when the likelihood of finding minimal or reversible coronary vascular disease is high."

Specifically, the examinations revealed that elevated blood pressure was correlated with excess body weight, a family history of risk factors (heart disease, hypertension, hyperlipidemia), and elevated levels of serum triglycerides and serum cholesterol.

The incidence of hypertension was greater among men than among women, and the correlation between elevated blood pressure and the other risk factors also proved stronger for the men.

Noting that blood pressure, obesity, and elevated serum lipids "are all alterable risk factors," the investigators suggest that early detection and modification of such conditions "should be the goal in this young population."

Co-authors were Dr. Antoni F. Salei, Chris Lyke, Caroline K. Clifford, Ph.D., Jess Kraus, Ph.D., Thomas Y. Cooper, and Drs. Nemat O. Borhani and Dean T. Mason.

## EDITORIAL CAPSULES

... brief summaries of editorials or comments in current medical and scientific journals.

### Impact Boondoggle

"The demand for 'impact statements' evaluating the environmental consequences of human activities in natural ecosystems seemed a natural outgrowth of the rise in ecological awareness of the 1960's. I believe that the idea has backfired."

"Many politicians have been quick to grasp that the quickest way to silence critical 'ecofreaks' is to allocate a small proportion of funds for any engineering project for ecological studies. Someone is inevitably available to receive these funds, conduct the studies regardless of how quickly results are demanded, write large, diffuse reports containing reams of uninterpreted and incomplete descriptive data, and in some cases, construct 'predictive' models, irrespective of the quality of the data base. These reports have formed a 'gray literature' so diffuse, so voluminous, and so limited in distribution that its conclusions and recommendations are never scrutinized by the scientific community at large. Often the author's only scientific credentials are an impressive title in a government agency, university, or consulting firm. This title, the mass of the report, the author's salary, and his dress and bearing often carry more weight with the commission or study board to whom the statement is presented than either his scientific competence or the validity of his scientific investigation. Indeed, many agencies have found it in their best interests to employ a 'traveling circus' of 'scientists' with credentials matching these requirements. As a result, impact statements seldom receive the hard scrutiny that follows the publication of scientific findings in a reputable scientific journal."

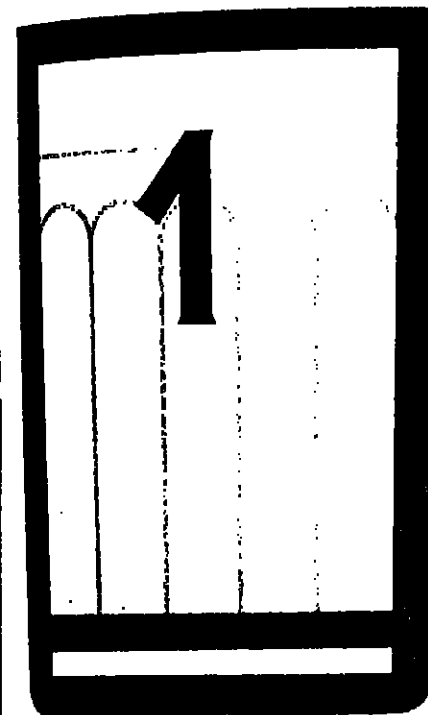
"The continued application of such studies can have several effects, including increased prices for natural resources; a declining credibility for environmental science and scientists; a reduction in the overall quality of scientific personnel; and the degradation of our natural resources, not as the result of the direct activities of industry and government, but because of the ineffectual groping of environmental scientists." (Editorial, D. W. SCHINDLER, *Science* 192:509, May 7, 1976).

"The continued application of such studies can have several effects, including increased prices for natural resources; a declining credibility for environmental science and scientists; a reduction in the overall quality of scientific personnel; and the degradation of our natural resources, not as the result of the direct activities of industry and government, but because of the ineffectual groping of environmental scientists." (Editorial, D. W. SCHINDLER, *Science* 192:509, May 7, 1976).

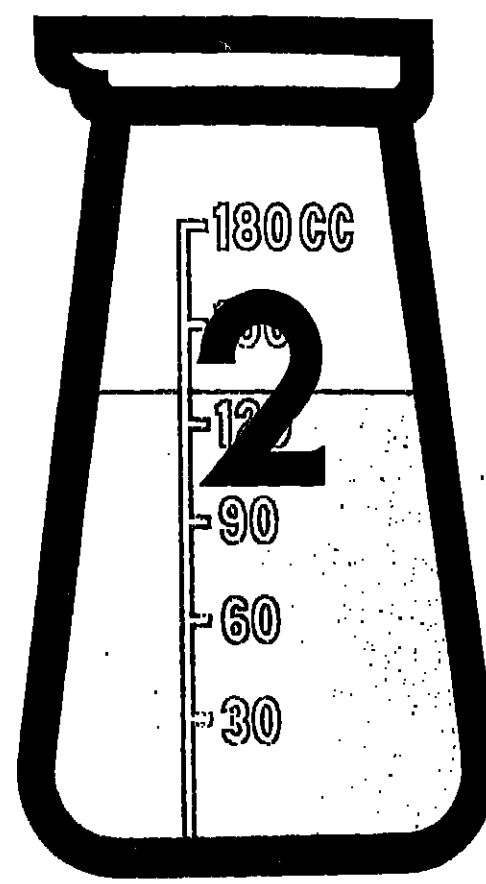
### New Drug Lowers Plasma Cholesterol, Triglycerides

Medical Tribune Report

ANAHEIM, CALIF.—A new drug, gemcadiol, has reduced blood plasma cholesterol and triglycerides in laboratory animals, according to Dr. Gertrude Rodney, a pharmacologist at the Park-Davis research laboratories. Dr. Rodney told the recent annual meeting here of the Federation of American Societies for Experimental Biology, that gemcadiol had "lowered the plasma triglycerides 90% in hypertriglyceridemic rats at a dose of 25 mg/kg per day."



Adequate fluid intake



Frequent voiding

# The 3rd Basic

## Gantanol® (sulfamethoxazole) B.I.D.

4 tablets (0.5 Gm each) STAT—then  
2 tablets B.I.D. for 10-14 days

Basic therapy with  
convenience for acute  
nonobstructed cystitis

• Effective against susceptible *E. coli*, *Klebsiella*, *Aerobacter*, *Staph. aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, cystitis and cystitis) due to susceptible organisms.

Notes: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminoglycoside acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of sulfonamides including sulfamethoxazole, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical

signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma, in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); allergic reactions (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photostress reactions (nausea, emesis, myocarditis); gastrointestinal reactions (nausea, vomiting, abdominal pain, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); CNS reactions (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); miscellaneous reactions (drug fever, chills, toxic nephrosis with oliguria and anuria, periarthritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm b.i.d. or t.i.d. depending on severity of infection. Usual child's dosage: 0.5 Gm (1 tab or teasp.) / 20 lbs of body weight initially, then 0.25 Gm / 20 lbs b.i.d. Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

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Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

### Manipulator Offers New Freedom



Bedside work table with manipulator arm permits quadriplegic to feed himself, select magazines from rack, turn pages, use a typewriter, and dial telephone. Developed at the Johns Hopkins Applied Physics Laboratory, the manipulator is activated by a faint twitch of the right shoulder muscle.

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## In Consultation

## Are Physicians Knowledgeable About Allergy to Insects?

Continued from page 6

but they should be trained in its use and in the recognition of symptoms of systemic reaction to insects. I am aware that this would probably entail changes in legislation as well as in thinking to allow a layman to inject epinephrine without fear of legal repercussions. I believe, however, that the annual toll of fatalities, most of them needless, warrants such legal and mental changes.

How can the allergic patient obtain such a kit?

I believe that in most, if not in all states, he must have the kit prescribed by his doctor. Thus, it is up to physicians to see to it that their vulnerable patients are protected. Physicians, however, should do more than prescribe. They should instruct their patients in how to use the kit. They should also point out that the epinephrine must be replaced when the liquid turns brown.

Who should receive hyposensitization?

Any individual who has suffered a systemic reaction to an insect sting or bite (if it is determined in the latter case that hyposensitization can afford protection), or if an individual has suffered a severe local reaction with considerable edema at the sting or bite site; i.e., swelling that extends from one joint to another if the patient is stung on an extremity.

How long should the patient receive a maintenance dose once the hyposensitization procedure has been completed and his tolerance level raised?

We used to think that three years was long enough. Some allergists now recommend 10 years. At the moment, with our present state of knowledge, or rather lack of it, I recommend that the patient be maintained indefinitely. Perhaps such a measure will be unnecessary in the future when we have more information about what it takes to acquire and maintain immunity. It is possible that we will discover that immunity is a highly individual matter and that we will be able to tailor our procedures to individual patients. In the meantime, I believe that safety is best.

What is the present status of hyposensitization with insect venom extract versus whole body extract?

The matter is somewhat academic still as far as desensitizing the patient is concerned, although bee venom extract is obtainable in some quantity for

diagnostic purposes. When queried, several commercial laboratories informed me that while supplies of bee venom will be ample, the venom of other insects is not only difficult to collect but will also be costly.

They also stated that they are still conducting tests regarding both the efficacy and safety of venom extracts and will not have sufficient data for another two or three years. The commercial laboratories contacted agreed that venom extract will probably be more expensive than WBE. It is apparent that more research must be done before venom extracts appear commercially and in quantity.

In the meantime, is whole body extract effective in hyposensitization? I believe it offers adequate protection when the patient can arrive at a

tolerance of 1:10 and is then maintained on such a dose every seven days from April 15 until October 15, and then increasing the interval to every two or three weeks. I have had no failures among my patients who have been resting after receiving this regimen.

What is a normal reaction to an insect sting and how do you treat it?

A normal reaction consists of a pin prick of pain, redness at the site gradually surrounded by a whitish zone and, often, a reddish flare. After a wheal forms and subsides, the area may feel irritated, itch, and exhibit some heat.

Treatment consists of scraping out the stinger and venom sac, if they remain in the wound, and washing thoroughly with soap and water.

Continued Next Issue

# Lasix Tablets (furosemide) 20mg and 40mg in hypertension.

Lasix Tablets have been shown to reduce elevated blood pressure in diuretic-responsive patients.

Lasix. For the treatment of essential benign hypertension.

## Acupuncture Offered to Nerve Deaf Children

Medical Tribune Report

Children between the ages of 9 and 17 suffering from nerve deafness are invited to participate in research evaluating the use of acupuncture. The research is being conducted at the Hearing Center of the Mount Sinai School of Medicine in New York City. The protocol has been reviewed and approved by the Human Subject Research Committee. No fee of any kind will be charged.

Physicians treating such children are requested by the Hearing Center to bring this to the attention of their patients and their families. Those who are interested can arrange for a preliminary interview by writing to P.O. Box 596, Lenox Hill Station, N.Y., N.Y. 10021, and giving name, age, address and phone number. Alternatively, an appointment can be arranged by calling (212) 288-7225.

## Gynecologist Cites 'Over-Reaction' To News of Ca Risk from Estrogen

Continued from page 1

Dr. Felix Rutledge said that "journalistic sensationalism" and FDA "promulgations" have "frightened women into premature action and placed an unnecessary burden on physicians to explain their practice."

Dr. Rutledge, who is Head of the Department of Gynecology at M.D. Anderson Hospital, Houston, Tex., said he believes the data are not all in and that meanwhile, women should not be deprived of estrogen therapy when it is indicated. "We should continue to provide patients relief of postmenopausal symptoms rather than surrender them to suffering because of the cancer

scare," he said. Amounts should be small, and administered to selected patients, he said, and patients should be carefully monitored.

## Weak Design

"If estrogen therapy increases the risk of endometrial cancer," Dr. Rutledge continued, "extensive use of these drugs should have produced a rise in the incidence of endometrial cancer nationally." But, he noted, "a stable incidence of endometrial cancer indicated by the Third National Survey is not consistent with a significant carcinogenic role for exogenous hormones, and this discrepancy needs resolution."

Further, Dr. Rutledge said, he believes the reports that estrogens increase the risk factor for endometrial cancer have "weaknesses in design," and that "confirmation must come from analysis of experiences of other centers well distributed geographically."

For example, he said, "The appropriateness of the patients for controls in the Washington-Seattle study should be criticized. Frequency in this study of estrogen replacement therapy for patients with endometrial carcinoma was compared with estrogen use in patients treated for cancer of the cervix, ovary, and vulva."

"The personal and health characteristics are notably different from the patient prone to develop carcinoma of the corpus. Therefore, the groups are not basically comparable."

On the other hand, Dr. Rutledge

said, attention must be directed to resolving the question of whether cancer of the endometrium is increasing, and if exogenous estrogens are responsible, and well-planned, prospective studies should be designed. For now, though, said Dr. Rutledge, "It seems prudent to regard replacement therapy with concern and to advise more judicious dispensing of these drugs while the questions are being investigated." But, he added, "We cannot cause clinicians to abandon these treatments."

## Risk vs. Benefit

The estrogens are important in the prevention of bone demineralization, Dr. Rutledge said, and only small amounts are needed. Similarly, small, spaced doses of estrogens will control severe vasomotor symptoms of "hot flashes." And patients with atrophic vaginitis may avoid systemic effects of estrogen by using vaginal creams containing the drugs. "Although there is some absorption, the amount is small," Dr. Rutledge noted.

"Physicians who must provide for postmenopausal women deserve an accurate risk-benefit assessment so that they can individualize patient care," Dr. Rutledge concluded.

Dr. David G. Decker, Professor and Chairman of Obstetrics and Gynecology at the Mayo Clinic, said he, too, is continuing to give estrogen therapy, but only for hot flashes, and in very small doses. "A dose level of 2.5 mg was the level implicated in the Olmstead study," he told MEDICAL TRIBUNE, and he said he does believe prolonged therapy increases the risk of endometrial cancer.

But for women who are "incapacitated" by hot flashes, Dr. Decker said he administers estrogens starting with a dose level of 0.625 mg and raising it to 1.25 mg if necessary, giving it in interrupted fashion for three out of four weeks.

## Histoplasmosis Traced To Bird Droppings

Medical Tribune Report

NEW ORLEANS—An epidemic of histoplasmosis that affected at least 68 persons in Hot Springs, Ark., has been traced to the wrong kind of civic clean-up—when workmen scraped old bird droppings from the courthouse tower, they just dumped the debris over the roof edge and down past rows of window air conditioners.

Histoplasma spores in the composted material were apparently sucked into the building through the air conditioners, Dr. Andrew G. Dean reported here to the joint meeting of the American Lung Association and its medical section, the American Thoracic Society.

Dr. Dean, who is acting director of the division of communicable diseases of the Arkansas State Health Department, said that 44 of the 84 employees inside the courthouse on the day of the dumping developed symptoms of histoplasmosis. Almost two-thirds of the people in offices adjacent to the wall behind the drop were infected.

Other victims included the two men who cleaned off the tower, several construction employees, and 10 townspeople who had visited the courthouse.

## A brief summary of the Prescribing Information for

Lasix® (furosemide) Tablets 20 mg and 40 mg

**WARNING:**—Lasix (furosemide) is a potent diuretic which if given in excessive amounts can lead to a profound diuresis with water and electrolyte depletion. Therefore, careful medical supervision is required, and dose and schedule have to be adjusted to the individual patient's needs. (See under "Dosage and Administration.")

**Indications:**—Lasix (furosemide) is indicated for the treatment of the edema associated with congestive heart failure, cirrhosis of the liver, and renal disease, including the nephrotic syndrome.

**Hypertension:**—Lasix (furosemide) may be used for the treatment of hypertension alone or in combination with other antihypertensive drugs. Hypertensive patients who cannot be adequately controlled with thiazides will probably also not be adequately controlled with Lasix (furosemide) alone.

**CONTRAINDICATIONS:**—Because animal reproductive studies have shown that Lasix (furosemide) may cause fetal abnormalities, the drug is contraindicated in women of childbearing potential. (See "Additional Information.") Lasix (furosemide) is contraindicated in anuria. If increasing anuria and oliguria occur during treatment of severe congestive heart failure, the drug should be discontinued. In hepatic coma and in states of extreme dehydration, therapy should not be instituted until the basic condition is improved or corrected. Lasix (furosemide) is contraindicated in patients with a history of hypersensitivity to this compound.

**Warnings:**—Excessive diuresis may result in dehydration and renal blood flow volume, with circulatory collapse and with the possibility of acute tubular necrosis and renal shutdown, particularly in elderly patients. Excessive loss of potassium in patients receiving diuretic therapy may precipitate digitalis toxicity. Care should also be exercised in patients receiving potassium-depleting diuretics. Frequent serum electrolyte, pH, and BUN determinations should be performed during the first few months of therapy and periodically thereafter, and abnormalities corrected or the drug temporarily withheld.

In patients with hepatic cirrhosis and ascites, initiation of therapy with Lasix (furosemide) is best carried out in the hospital. Such an approach allows a close watch on the patient's status, and a rapid reduction in hepatic congestion, therefore, should be observed during the period of therapy. Supplemental potassium chloride and, if required, an aldosterone antagonist are helpful in preventing hypokalemia and metabolic alkalosis.

Patients should be observed regularly for the possible occurrence of blood dyscrasias, liver damage, or other idiosyncratic reactions.

In those instances where potassium supplementations are required, an oral liquid preparation should be used rather than enteric-coated potassium salts. There have been several reports, published and unpublished, concerning non-specific small-bowel lesions consisting of stenosis, with or without ulceration, associated with the administration of enteric-coated tablets with potassium salts. These lesions may occur with enteric-coated potassium tablets when they are used with nonenteric-coated thiazides, or with other oral diuretics.

These small-bowel lesions have caused obstruction, hemorrhage, and perforation. Surgery was frequently required, and deaths have occurred. Available information indicates that enteric-coated potassium salts, although lesions of this type also occur sporadically. Therefore, enteric-coated potassium-containing preparations should be administered only when indicated and should be discontinued immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occurs.

Patients with known sulfonamide sensitivity may show allergic reactions to Lasix (furosemide).

**Precautions:**—As with any potent diuretic, electrolyte depletion may occur during therapy with Lasix (furosemide), especially in patients receiving high doses and in patients with severe dehydration. Electrolyte depletion may manifest itself as weakness, dizziness, fatigue, leg cramps, anorexia, vomiting, and/or mental confusion.

Asymptomatic hypokalemia can occur and may rarely be precipitated by reversible elevations of BUN. It may be seen. There have been reports of association with dehydration, which should be avoided, particularly in patients with renal insufficiency.

When parenteral use of Lasix (furosemide) precedes its oral use, it should be kept in mind that cases of benign and reversible hearing impairment have been reported. There have also been some reports of cases of irreversible hearing impairment. Usually, ototoxicity has been reported when Lasix (furosemide) was administered in patients with severe impairment of renal function at doses exceeding the usual recommended dose and in whom other drugs known to be ototoxic were being given. If the diuretic effect is to be used in patients with severe renal impairment, it has been reported that an infusion rate not exceeding 4 mg Lasix (furosemide) per minute has been used.

Increases in blood glucose and antecipatory glucose tolerance tests with administration of the drug and two-hour postprandial sugar have been observed. No dose effect on precipitation of diabetes mellitus has been reported.

Lasix (furosemide) may lower serum calcium levels, and rare cases of tetany have been reported.

Patients receiving high doses of salicylates, in conjunction with Lasix (furosemide) may experience salicylate toxicity at lower doses because of competitive renal excretory sites.

Drugs such as furosemide may enhance the nephrotoxicity of cephalosporins. Therefore, Lasix (furosemide) and cephalosporins should not be administered simultaneously.

Sulfonamide diuretics have been reported to decrease internal responsiveness to pressor amines and to enhance the effect of tubocurarine. Great caution should be

exercised in administering curar or its derivatives to patients undergoing therapy with Lasix (furosemide), and it is advisable to discontinue Lasix (furosemide) for one week prior to any elective surgery.

**Adverse Reactions:**—Various forms of dermatitis, including urticaria and rare forms of exfoliative dermatitis, erythema multiforme, pruritus, paronychia, burning or vision, retinopathy, hypotension, nausea, vomiting, or diarrhea.

Anemia, leukopenia, aplastic anemia, and thrombocytopenia (with purpura). Rare cases of agranulocytosis have been reported; however, the relationship to the drug has not been established with certainty. Sweet's syndrome, and gastric burning, paralytic ileus, headache, jaundice, thrombophlebitis and embolism and acute pancreatitis.

Lasix (furosemide)-induced diuresis may be accompanied by weakness, fatigue, lightheadedness or dizziness, muscle cramps, thirst, increased perspiration, urinary bladder spasm, and symptoms of urinary frequency.

## Dosage and Administration

**Adults:**—The usual adult dose of Lasix (furosemide) is 20 to 80 mg given as a single dose. The diuretic response with a single dose of 20 to 80 mg is not satisfactory, the following schedule should be used: Increase this dose by increments of 20 or 40 mg until a satisfactory diuretic effect is obtained. The diuretic effect should be maintained by giving the drug at intervals of 6 to 8 hours after the previous dose until the desired diuretic effect has been obtained. This individually determined single dose should then be given once or twice daily. The dose of Lasix (furosemide) may be carefully titrated up to 800 mg per day in those patients with severe clinical edematous states.

With doses exceeding 80 mg/day and given for prolonged periods, careful clinical

and laboratory observations are particularly advisable.

**Hypertension:**—The usual dose of Lasix (furosemide) is 40 mg twice daily both for initial therapy and for maintenance. Careful observations for changes in blood pressure must be made when this compound is used with other antihypertensive drugs. If necessary, the dosage of other agents must be reduced by 50 percent as soon as Lasix (furosemide) is added to the regimen to prevent hypotension. As the blood pressure falls under the potentiation of Lasix (furosemide), a further reduction in dosage, or even discontinuation, of other antihypertensive drugs may be necessary. It is further recommended that 140 mg twice daily does not lead to a clinically satisfactory response, to add other hypotensive agents, e.g., reserpine, rather than to increase the dose of Lasix (furosemide).

**Infants and Children:**—The usual initial dose of oral Lasix in infants and children is 2 mg/kg body weight, given as a single dose. If the diuretic response is not satisfactory after the initial dose, dosage may be increased by 1 or 2 mg/kg not more than 6 to 8 hours after the previous dose. Doses greater than 6 mg/kg body weight are not recommended.

For maintenance therapy in infants and children, the dose should be adjusted to the minimum effective level.

**How Supplied:**—Lasix Tablets 40 mg (furosemide) supplied as white, round, monogrammed, scored tablets.

Lasix Tablets 20 mg (furosemide) supplied as white, oval, monogrammed tablets.

**Pack:** Dispense in dark containers. Exposure to light may cause slight discoloration which, however, does not alter potency.

**Additional Information:**—Lasix (furosemide) has been determined in mice, rats, and dogs. In all three animal species, the oral LD<sub>50</sub> of Lasix (furosemide) exceeded 1000 mg/kg of body weight, while the intravenous LD<sub>50</sub> ranged from 300 to 600 mg/kg.

The acute toxicity of the drug in newborn rats resulted in an LD<sub>50</sub> of 360 mg/kg. The acute toxicity of high doses of Lasix (furosemide) was characterized by intragastric injection of the drug in newborn rats became dehydrated and anorectic.

The results of the acute toxicity studies with Lasix (furosemide) in the convulsions, paralysis, and ataxia. Surviving animals often became dehydrated and anorectic. In newborn rats, intragastric injection of the drug caused hyperactivity and anorexia.

Chronic toxicity studies with Lasix (furosemide) were done in mice and dogs. A one-year study in mice, renal tubular degeneration occurred, with evidence higher than 50 mg/kg (4 times the maximal recommended human dose of 600 mg per day).

The results of the chronic toxicity studies and of the renal parenchyma at six-month study in dogs revealed calcification and scarring of the renal parenchyma at doses above 10 mg/kg (33 percent of the maximal recommended human dose of 600 mg per day).

**Reproductive Studies:**—The effects of Lasix (furosemide) on embryonic and fetal development and on reproductive studies in mice, rats, and rabbits.

Lasix (furosemide) caused unexplained maternal deaths and abortions in the pregnant dams were studied in mice, rats, and rabbits. In a previous study the rabbit was administered Lasix (furosemide) at a dose of 600 mg/kg (12 times the maximal recommended human dose of 600 mg per day) was administered between days 12 to 17 of gestation. In a previous study the lowest dose of only 25 mg/kg (2 times the maximal recommended human dose of 600 mg per day) caused maternal deaths and abortions. In a third study, none of the pregnant rabbits survived a dose of 100 mg/kg. Data from the above studies indicate that Lasix (furosemide) can produce maternal death.

Results of the toxicity studies and one of the above rabbit studies also showed a fetal lethality which can produce resorption of the fetus in the uterus. In some cases, the results of the toxicity studies and one of the above rabbit studies also showed an increased incidence of hydronephrosis and scarring of the renal parenchyma at doses of 10 mg/kg (33 percent of the maximal recommended human dose of 600 mg per day).

Incidence in fetuses from the control group.

**HOECHST-ROUSSEL**  
PHARMACEUTICALS INCORPORATED  
SOMERVILLE, NEW JERSEY 08876

HOECHST-ROUSSEL

## "I GOT LOST- LOST IN MY OWN NEIGHBORHOOD"

Yesterday I was going to the grocery store and suddenly I didn't know the way. I was all mixed up. I thought it was the old neighborhood. It frightened me—and it's not the first time. My children say it's my second childhood. Well, it's not. I took care of my children. Please, doctor.

## WHEN "GRAY AREA" SYMPTOMS START TO AFFECT THE ELDERLY PATIENT'S LIFE

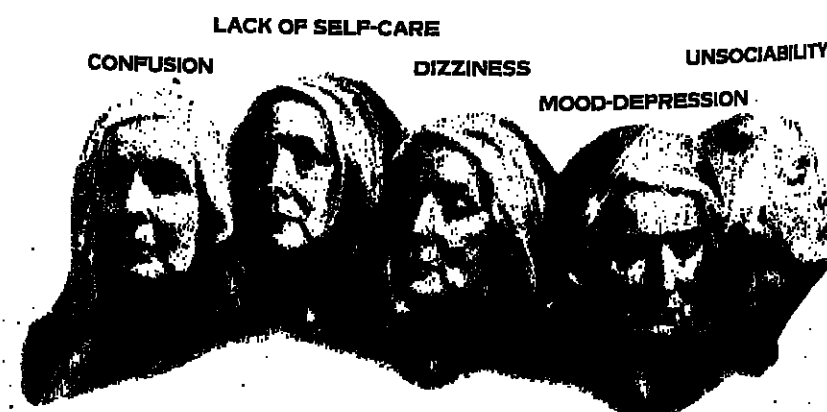
A SINGLE 1-mg HYDERGINE SUBLINGUAL  
TABLET THREE TIMES A DAY.

- Meets the proper 3-mg total daily dose of Hydergine therapy.
- Makes compliance easier for patients who might be confused by more complicated schedules.
- Helps assure optimal dosage because of better adherence to dosage regimen.
- Oval shape of 1-mg tablet makes it easier for the elderly patient to identify.

**Contraindications:** Hypersensitivity to the drug.  
**Precautions:** Because the target symptoms are of unknown etiology, careful diagnosis should be attempted before prescribing Hydergine sublingual tablets.

**Adverse Reactions:** Serious side effects have not been found. Some sublingual irritation, transient nausea, and gastric disturbances have been reported. Hydergine sublingual tablets do not possess the vasoconstrictor properties of natural ergot alkaloids.

**Dosage and Administration:** 1 mg sublingually three times daily. Alleviation of symptoms is usually gradual and results may not be observed for 3-4 weeks.



GIVE ENOUGH, SOON ENOUGH  
LONG ENOUGH

## HYDERGINE 1mg

Each 1-mg Hydergine sublingual tablet contains dihydroergocornine 0.333 mg, dihydroergocristine 0.333 mg, and dihydroergokryptine 0.333 mg, as the mesylates, representing a total of 1.0 mg.

SANDOZ PHARMACEUTICALS, EAST HANOVER, NEW JERSEY 07936

Wednesday, July 7, 1976

MEDICAL TRIBUNE

11

The Only Independent Weekly Medical Newspaper in the U.S.

# Medical Tribune

and Medical News  
Published by Medical Tribune, Inc.

## Placebo Effects

A MEMBER OF THE DEPARTMENT OF PHILOSOPHY at the University of Arizona, Henry Byerly, Ph.D., recently directed his philosophical eye to the matter of placebos. In the Spring issue of *Perspectives in Biology and Medicine*, Dr. Byerly's article on "Explaining and Exploiting Placebo Effects" concentrates mostly on the explanation. And this turns out to be a survey of the varied explanations that have been proffered over the years for the effects of what Dr. Henry Beecher more than twenty years ago termed "The Powerful Placebo." As Dr. Byerly notes, we are still awaiting "definitive explanations."

In the absence of definitive explanations, Dr. Byerly writes, "The curative efficacy of placebos can be interpreted in four different ways if we distinguish 'real' organic disease from 'imaginary' or merely psychological symptoms: (1) Placebos can effect real cures of real diseases. (2) Placebos can effect real cures of imaginary diseases. (3) Placebos can effect imaginary cures of real diseases. (4) Placebos can effect imaginary cures of imaginary diseases. According to (1), placebos can function as surrogates for effective drugs in removing physiological causes of illnesses. According to (2), placebos have efficacy only in removing psychological symptoms. On interpretation (3), placebos merely relieve symp-

toms where there are organic causes. The last possibility (4) relegates the efficacy of placebos to removing subjective symptoms where there is no organic disease."

What is most interesting in Dr. Byerly's article is its final few lines, which are devoted to the question of how placebos should be exploited even in the absence of definitive explanations. He expresses surprise at the flat recommendation by some physicians that placebos ought never to be used because of the apparent fear that mere symptoms would be treated as opposed to "real causes." Dr. Byerly, on the other hand, opts for conscious use of placebo effects to relieve symptoms where possible and appropriate.

It seems likely that even physicians who deplore the use of placebos and view them as inconsistent with true medical care are nonetheless utilizing the most powerful placebo extant. That is the physician himself. The physician himself secures true physiological responses in his patient and does so for better or for worse. A physician who is enthusiastic about a procedure or a medication is likely to evoke better results than the doubter or the skeptic. And the physician who lets fall within earshot of a patient a truly discouraging remark or even one that may be so interpreted can create havoc and true disaster.

## More on Malpractice

THE NEWS THAT A CIRCUIT COURT JURY in the Chicago area awarded damages to a physician who counter-sued a patient and her attorneys for bringing a malpractice suit against him without a reasonable cause (see pp. 1, 4) has been electrifying to members of the medical profession. The \$8,000 awarded to Dr. Leonard Berlin—\$2,000 in compensatory damages and \$6,000 in punitive damages—is minuscule in comparison to the sums awarded to patients and their attorneys in malpractice cases. But the success of Dr. Berlin is so unexpected that it falls in the category of "man bites dog."

However, the fact that Dr. Berlin "spent \$10,000" of his own funds and "25 working days" in pursuit of justice demonstrates one reason why insurance companies prefer to settle malpractice cases even when they have no merit. It is cheaper for them to do so. On Feb. 11, an editorial in *MEDICAL*

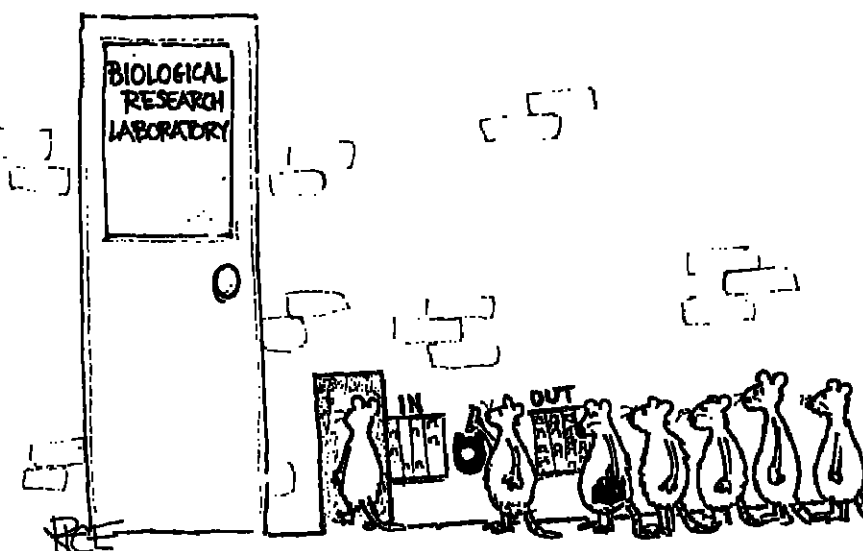
*TRIBUNE* applauded a physician who had sued six insurance companies for a total sum exceeding \$5,000,000. The insurance companies had offered to settle a malpractice case against him for \$12,000 over the protests of the physician who insisted that the claim was invalid. The case did go to a jury that found no malpractice had been committed. With this, the physician instituted suit against the insurance companies, asserting that their investigations of the case against him were "negligent to such a degree as to constitute a wilful and wanton disregard" of his professional reputation, his financial interests and his standing in the community as well.

We do not know the outcome of that case but not only patients and their attorneys ought to be put on warning about frivolous malpractice suits; the insurance companies should share in this warning as well.

## Alcoholic Bio-Marker

CLINICAL QUOTE: "This is the first time a biochemical marker for alcoholism has been reported. We have here a possible handle on the problem of alcoholism. We've never before been

able to say what makes an alcoholic different from a nonalcoholic. Here we have a biochemical difference." (Dr. Charles S. Lieber, Mt. Sinai School of Medicine. See page 3.)



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## LETTERS TO TRIBUNE

### On Vasectomy

I admire most of what Dr. Arthur Sackler writes in his "One Man and Medicine" column. In the April 17, 1976 issue, however, I think he got things backward when he said that when you offer vasectomy to a broad population the highly responsible socially conscious individuals with good education will respond, and those socially immature (for many reasons) will refuse to participate, thus inverting eugenics.

I submit that the socially responsible are already limiting their pregnancies, and that mass programs must be aimed toward involving the others.  
DAVID PLATT, M.D.  
Wilmington, Del.

### On Abuse of the Press

I am writing to compliment Dr. Sackler for his column [on abuse of the press and science, MT, Mar. 17]. I welcome especially the quote from Thomas Jefferson which began your editorial.

Near the end of my term as President of the Nebraska Medical Association, I am acutely aware of the licentiousness of the press. I have long believed, and have come to believe even more strongly this year, that the press betrays the First Amendment nearly consistently. I believe that that Amendment was intended by its writers to assure the citizens access to knowledge about the government and to make sure that governments did indeed operate in the clear light of Truth. Apparently from the beginning, the press took advantage of this, which advantage has become worse as the news media have expanded their capabilities and technology.

I have resented the manner in which these news-gatherers mis-state the truth and mis-represent the position and statements of medicine. We are nearing the end of a long and arduous effort to have corrective legislation for medical liability passed by our Legislature. I believe now that we shall be successful, but you can well imagine the field day that various elements of the press have had with this.

I have been much pleased by the editorials in *Science* in the past several months, and I hope that they will indeed mobilize all of the scientific community to the dangers of the government attack on medicine and, of course, to science generally.

I shall enjoy very much showing your editorial to various of my "friends" in the newspaper and radio industry.

WARREN BOSLEY, M.D., President  
Nebraska Medical Association  
Grand Island, Nebraska 68801

Your article on "The Abuse of the Press—and of Science" is an eloquent and badly needed comment on a situation that cannot be allowed to continue indefinitely. It is rapidly destroying the basic glue which is essential for the life of a free society—a reasonable degree of belief and confidence in the essential integrity of one's fellow citizens.

I would like to have another copy of the article so that I can reproduce it and give it to my patients and others (the label covered a part of the article). I also suggest *MEDICAL TRIBUNE* start producing reprints of this and other articles on malpractice, etc., for distribution in doctors' offices. The medical profession, for a variety of reasons, is probably incapable of communicating effectively enough by means of the mass media; effectively enough to really counter the careless and sometimes malicious charges which are so frequently hurled at the profession.

I believe *MEDICAL TRIBUNE* could, and hope it will, provide the leadership to bring about an ongoing communication program that will be strong enough to counter the libels that are so constantly being made in these times.

JOSEPH W. STILL, M.D., M.P.H.

### Correction

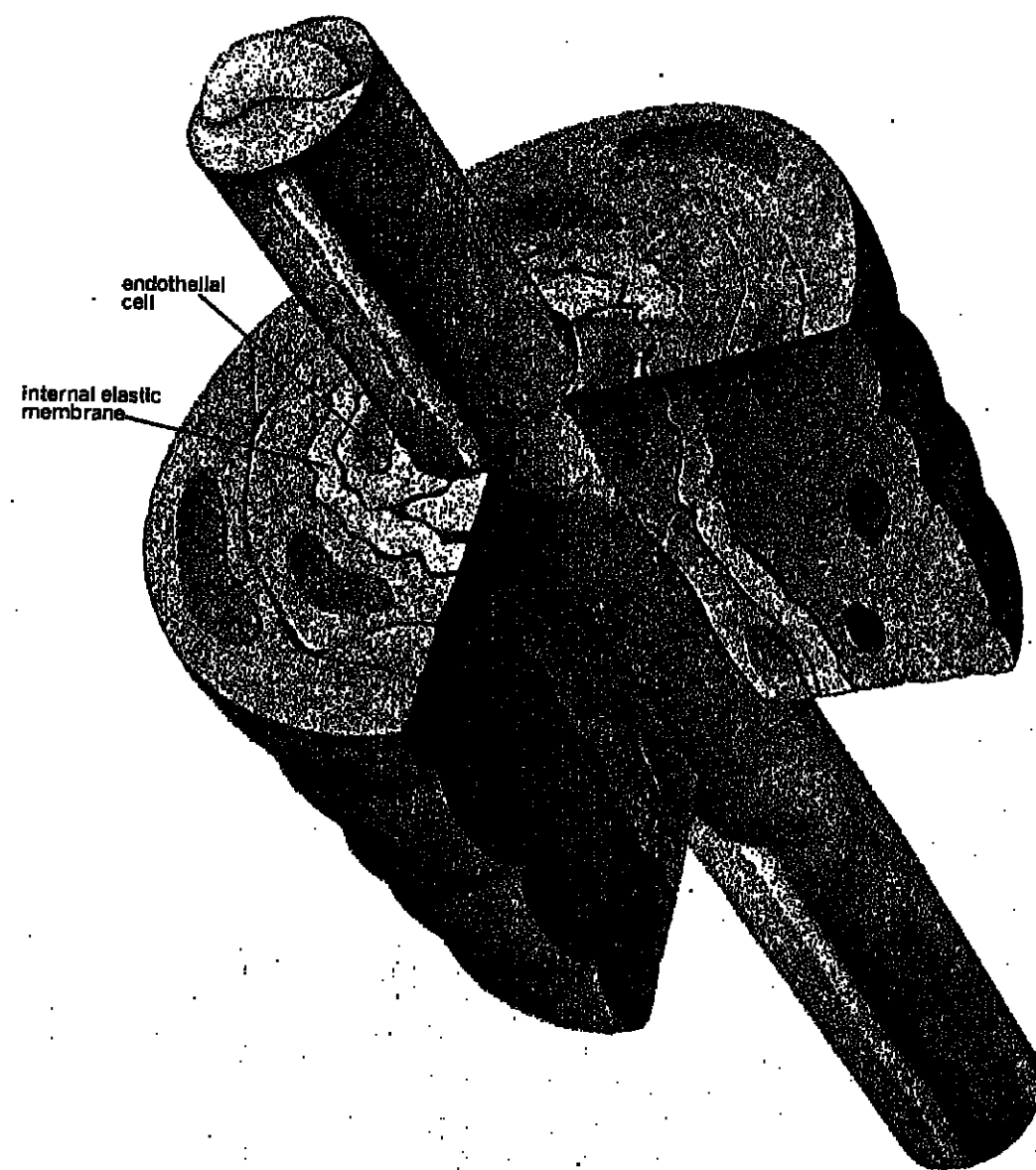
A photo caption in The Good Drugs Do in fighting arthritis section (MT, May 12) erroneously identified Dr. Howard E. Skipper, Lasker Award winner for his studies of metabolism of anti-cancer drugs, as another winner, Dr. John Charnley. Our apologies—Editor.



# Apresoline... (hydralazine) relaxes arterioles to solve the major hemodynamic problem in hypertension

Abnormally high peripheral resistance is the major hemodynamic problem with most hypertensives.

Apresoline reduces peripheral resistance and lowers blood pressure through a direct relaxation of arteriolar smooth muscle.



## high peripheral resistance: common attribute of most hypertensives

Because high peripheral resistance is the major hemodynamic disturbance found in most patients with essential hypertension,<sup>1,2</sup> the therapeutic goal should be reduction of total peripheral resistance and a return to more normal peripheral circulation.<sup>1,2</sup>

Hence, vasodilating drugs "...offer a physiologically rational approach to the therapy of hypertension."<sup>3</sup> In addition, "...vasodilators [combined with a sympathetic inhibitor] are the most predictable and specific drugs for reversing the hemodynamic abnormality of most hypertensive patients."<sup>4</sup>

## the only oral agent that deals directly with this problem

Apresoline (hydralazine), the only currently approved oral antihypertensive with vasodilating action, decreases peripheral resistance—regardless of its cause—and, hence, arterial pressure by relaxing arteriolar smooth muscle. Accompanying the fall in blood pressure is a rise in cardiac output and rate. Apresoline also maintains or increases renal and cerebral blood flow.

## a different and complementary pharmacologic approach

Different in action from all other oral antihypertensives and compatible with most of them, Apresoline can play a significant role in a variety of therapeutic combinations.

Such combinations, according to Freis,<sup>5</sup> with each component representing a different antihypertensive mechanism,

provide the most effective way to control blood pressure. This approach may also permit lower drug dosages.

## the problem of postural hypotension minimized

Nickerson<sup>6</sup> describes the action of Apresoline as follows:

"A preferential effect on arterioles, as compared to veins, allows the increase in cardiac output and minimizes postural hypotension; the latter is much less than that produced by agents blocking sympathetic nerves."

Continued on following page

### Apresoline<sup>®</sup> hydrochloride (hydralazine hydrochloride)

#### TABLETS

Essential hypertension, alone or as an adjunct.  
CONTRAINDICATIONS  
Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.

WARNINGS  
Hydralazine may produce in a few patients a clinical picture resembling systemic lupus erythematosus. In such patients hydralazine should be discontinued unless the benefit to be derived from antihypertensive therapy with hydralazine requires continued antihypertensive therapy with

this drug. Symptoms and signs usually regress when the drug is discontinued but residua have been detected many years later. Long-term treatment with steroids may be necessary.

Complete blood counts, L.E. cell preparations and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy even though patient is asymptomatic. These studies are also indicated in the presence of any unexplained symptoms.

A positive antinuclear antibody titer and/or positive L.E. cell reaction requires that the physician carefully weigh the implications of the test results against the benefits to be derived from antihypertensive therapy with hydralazine.

Use MAO inhibitors with caution.

#### Usage in Pregnancy

The drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.

#### PRECAUTIONS

Use cautiously in suspected coronary artery or other cardiovascular diseases, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.

Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antidopaminergic effect and addition of pyridoxine to the regimen if symptoms develop.

Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported rarely. If such abnormalities develop, discontinue

therapy. Periodic blood counts are advised during prolonged therapy.

#### ADVERSE REACTIONS

Common: Headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. Less frequent: Nasal congestion; flushing; irritation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremors; muscle cramps; psychologic reactions characterized by depression, disorientation, or anxiety; hypersensitivity (including rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia,

agranulocytosis, and purpura; hypotension; paradoxical pressor responses.

#### DOSEAGE

Initiate therapy in gradually increasing dosages: 10 mg 4 times daily for the first 2 to 4 days, increase to 25 mg 4 times daily for balance of first week. For second and subsequent weeks, increase dosage to 50 mg 4 times daily. For maintenance, adjust dosage to lowest effective level.

The incidence of toxic reactions, particularly the L.E. cell syndrome, is high in the group of patients receiving large doses of Apresoline.

In a few resistant patients, up to 300 mg Apresoline daily may be required for a significant antihypertensive effect. In such cases, a lower dosage of Apresoline combined with a thiazide, reserpine, or

both may be considered. However, when combining therapy, individual titration is essential to insure the lowest possible therapeutic dose of each drug.

HOW SUPPLIED  
Tablets, 10 mg (pale yellow, dry-coated); bottles of 30, 60, 100 and 1000.

Tablets, 25 mg (deep blue, dry-coated) and 50 mg (light blue, dry-coated); bottles of 30, 60, 100, 500 and 1000.

Tablets, 100 mg (peach, dry-coated); bottles of 100.

Consult complete literature before prescribing.

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C I B A

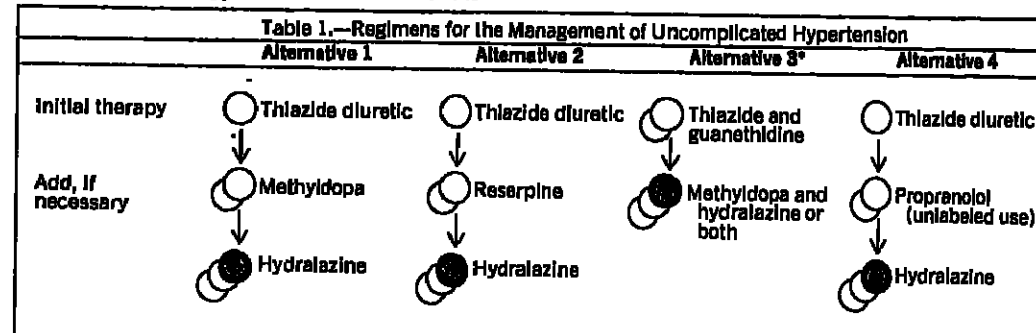
Julian Grist Project Manager  
John McKee Administration Manager  
Vicki Morison Administration Manager  
Isabel Hutchings Conference Manager  
Charlotte Benton-Hughes Conference Manager  
Technical Services

NR 332 2422  
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# Apresoline® (hydralazine)

## ...key component in the "guideline" antihypertensive regimens

AMA Committee on Hypertension Recommendations

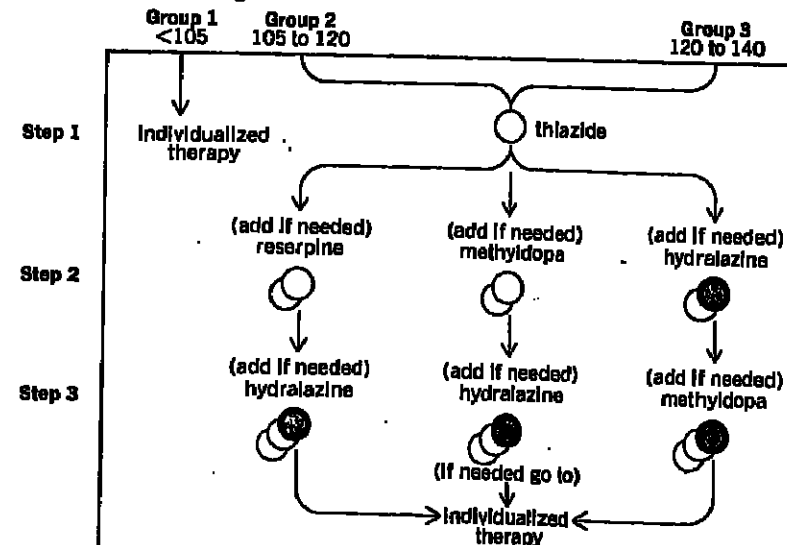


\*In patients who cannot tolerate guanethidine, alternatives 1 or 4 may be given a therapeutic trial, but treatment should be initiated with both the diuretic and methyldopa or propranolol.

**Apresoline...  
included in all four  
treatment plans by the  
AMA Committee\***

(Adapted\*)

Recommendations by the Hypertension Task Force of the National High Blood Pressure Education Program



Therapeutic Objective: Diastolic pressure under 90 mm Hg, or, if untoward effects cannot be tolerated, under 100 mm Hg.

**used effectively in the  
landmark VA  
studies<sup>8,9</sup>**

Apresoline was one of the three basic drugs used in two published VA cooperative studies—studies which demonstrated conclusively the benefits of antihypertensive treatment in reducing risk of morbidity and mortality.

**Apresoline®...  
(hydralazine)  
An antihypertensive  
idea whose time  
has come**



- References**
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  - Effects of treatment on morbidity in hypertension: Results in patients with diastolic blood pressures averaging 115 through 129 mm Hg. Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 202:1028-1034, 1967.
  - Effects of treatment on morbidity in hypertension: II. Results in patients with diastolic blood pressures averaging 90 through 114 mm Hg. Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 213:1143-1152, 1976.

**C I B A**

Wednesday, July 7, 1976

### Pediatric Progress

...brief summaries of editorials or comments in current medical and scientific journals.

#### Pediatric Hypertension

Increasing awareness that children and adolescents may be predisposed to or affected by hypertension is providing a rationale for inclusion of reliable blood pressure measurements in the physical examination of patients over 3 years of age and in selected younger children if a high index of suspicion exists.

Failure to recognize the presence of high blood pressure may result in delayed diagnosis, misdiagnosis, or inadvertent use of potentially harmful therapeutic agents. Furthermore, the outcome of many conditions associated with hypertension is favorably affected when antihypertensive therapy is given.

Finally, perhaps most important but most difficult to convey to affected individuals and to young physicians is the long-term benefit that may accrue from appropriate therapeutic intervention. These reasons create a strong argument for ensuring that the value of routine blood pressure measurement is taught during primary care training, to better professional practices that will improve patient care. (Patricia T. Rodin, M.A., et al, *JAMA* 235:2320, May 24, 1976)

#### Recognizing Renal Failure

Early recognition of renal failure is of great importance... The frequency of micturition, the volume, appearance, and composition of urine should be determined routinely in all high-risk infants. If possible, urine passed in the delivery room should be collected and analyzed; under normal circumstances the "first" urine is hypotonic. In most cases the condition of acute renal failure is considered reversible and is corrected when good oxygenation, a normal acid-base status, plasma volume, and circulation have been restored. Excessive excretion of sodium in utero or during the recovery phase from renal failure could lead to sodium depletion. If this occurs, oral or intravenous administration of sodium chloride might be indicated. Drugs used to control hypo- or hypertension which might reduce glomerular filtration should be used with great care. Peritoneal dialysis, which has been recommended as a valuable tool for the management of uremia, might be useful for acute renal failure in the immediate neonatal period. However, the most important treatment is prevention of asphyxia...

The reports of renal failure in the newborn infant probably represent only the most severe cases. In the light of recent investigations of renal function in the fetus, more moderate impairment of renal function very likely remains unrecognized and could well account for some of the "normal variation" noted in the newborn infant. (Guthrie S. Daniel, Ph.D., and L. Stanley James, M.D., *J. Pediatr.* 88:856, May, 1976)

MEDICAL TRIBUNE

15

## Gout Medication Found Effective in Treatment of Severe Cirrhosis

Continued from page 1

end of the initial two-year trial are showing the same benefits from colchicine therapy, said Dr. David Kershenovich, of the Department of Gastroenterology, National Institute of Nutrition, Mexico City.

The study was praised as "elegant and exciting" by Dr. Hans Popper, of Mt. Sinai School of Medicine, N.Y., who said the Mexican team's findings warrant further clinical investigation.

The double-blind trial followed a series of experimental studies showing that colchicine inhibited hepatic fibrosis and improved liver function in traumatized rats, Dr. Kershenovich reported. When a preliminary clinical study showed that colchicine could be useful in severely ill cirrhotic patients, the team undertook its two-year double-blind trial in 28 patients, about half of whom were alcoholics.

Treated patients received 1 mg of colchicine daily, five days a week for two years. Liver function tests were

performed monthly, and liver biopsies obtained every six months, examined double-blind and graded on a scale of 1-4 for inflammation and fibrosis. Dr. Kershenovich noted that, prior to treatment, 10 of 14 patients in the colchicine group and six of 14 in the placebo group had ascites, edema and bleeding esophageal varices. Encephalopathy was present in four of the treated group and in three of the placebo group. In all patients, there was pretrial histologic evidence of cirrhosis. The alcoholics in the series continued their usual drinking habits during the trial, the investigator said.

#### Treated Patients Alive

"After 24 months of treatment, all patients in the treated group were alive, without ascites and/or edema," Dr. Kershenovich declared. "No bleeding episodes had occurred and only one patient had encephalopathy. In contrast, no clinical improvement was seen in the placebo group and two pa-

tients died of the complications of cirrhosis. Gamma-globulins dropped from a mean of 3.9 to 3.1 g% in the colchicine group and remained elevated in the placebo series. Serum albumin remained unchanged in the treated patients, but decreased from 3.5 to 2.7g% in the placebo group." There were, however, no significant histologic changes in the liver biopsies of either group.

The resolution of clinical findings, the decrease in gamma-globulins and the maintenance of normal albumin levels, the investigator concluded, suggest that "colchicine may be of value in the treatment of cirrhotic patients."

He noted that the drug's mechanism of action in this series is still unclear. But Dr. Popper in discussion suggested that a penicillamine effect could be taking place, since penicillamine "may alter fibrous development in man and animals."

Coauthors were Drs. Manuel Uribe, C. I. Guarez, and M. Rojkind.

## Diet Being Studied as Explanation for Varied International Breast Ca Rates

Medical Tribune Report

LAS VEGAS, Nev.—Dietary differences, particularly in regard to fats, are now being looked at to explain international variations in breast cancer incidence.

Dr. Anthony B. Miller, director of the epidemiology unit of the National Cancer Institute of Canada and chairman of the epidemiology committee of the U.S. Breast Cancer Task Force, said here these differences constitute the "most favored hypothesis" at the present time.

Genetic factors, among others, have received wide attention, Dr. Miller noted, but they do not explain the changes that occur in groups that migrate. He pointed out that Japanese women have a comparatively low incidence of breast cancer in Japan, but that the incidence increases as they move to Hawaii and the U.S.

"Family history may be indicative of a genetic factor," Dr. Miller told a conference on Detection and Treatment of Early Breast Cancer, "but it might also indicate common exposure to an environmental factor."

#### Environment Important

A number of studies are aimed at identifying genetic markers, he added, "but if I were asked to bet which would come out, I would say that genetics will be pretty low and environmental factors will be much more important."

Epidemiologic factors are receiving intensive examination now for two reasons, Dr. Miller noted. One is concerned with possible prevention, the other—and perhaps more pressing—concern is with the populations that should receive intensive screening.

Right now, Dr. Miller said, even three or more of the commonly designated risk factors are not discriminatory enough to ascertain breast cancer risk with any degree of precision. However, he added, "We have to look at the premise of an annual examination for all women over age 50."

Paradoxically, Dr. Miller noted that the ultimate answers to the questions of risk factors may come from such screening, if demographic and epidemiologic questions are included in the examinations.

Meanwhile, encouraging results were reported at this meeting for such examinations when they include mammography. Participants in some of the 27 centers taking part in the Task Force demonstration projects reported an extremely high incidence of very early cancer detection, those considered small enough to be potentially "curable."

Among the more conclusive results to date came from the HIP Mammography Study, the only controlled study to date. Run by the Health Insurance Plan of Greater New York, it is now in its seventh year.

Mr. Sam Shapiro, a professor at the Johns Hopkins School of Hygiene and Public Health, and former director of research and statistics for HIP, said the HIP program has shown a one-third reduction in breast cancer mortality among women over age 50.

This study took two random samples, each of 31,000 women aged 40 to 64 who belonged to the prepaid insurance plan. The women in the study group were offered a screening examination—including history, clinical examination, and mammography—plus three additional examinations at annual intervals. The women in the control group followed their usual practices. No special effort was made to encourage them to have examinations, nor were they discouraged from having them.

The randomness of the two groups was later confirmed, Professor Shapiro said, by the fact that the breast cancer detection rate—299 in the study group, and 285 in the control group—and the overall mortality rate were similar.

This observation has to be taken with considerable caution, Professor

Shapiro pointed out, because "given the size of the population, the reduction in mortality for women under age 50 might easily have been missed."

Further, he said, there is the possibility that the results of such a study begun today might be even more encouraging because the radiologist of today "is far more effective" than the radiologist of years ago.

As for the risks of mammography, Prof. Shapiro said indications now are that "the radiogenic effects do not come close to the benefit."

#### Malaria Vaccine Hope



Hope for a vaccine against malaria has risen with discovery by Dr. William Trager, of Rockefeller University, of a way to culture the parasite *Plasmodium falciparum* in human erythrocytes. Photomicrograph, taken 75 days after culturing, shows parasites in various stages of development.

John McKee Project Manager  
Vicki Morrison Administration Manager  
Isabel Hutchings Conference Manager  
Charlotte Benton-Hughes Conference Assistant  
Technical Services Manager

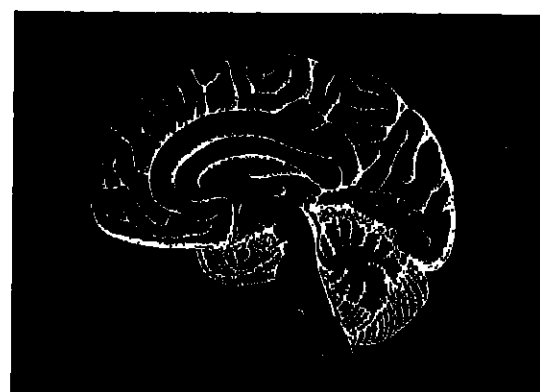
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Tel: 081 332 2422  
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# Are all antianxiety- anticholinergic therapies the same?

## Not if you know Librax.



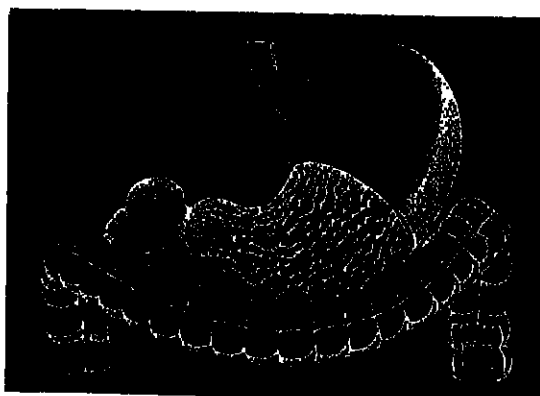
Only Librax provides

■ the well-known antianxiety action  
of Librium® (chlordiazepoxide HCl)

plus

■ the prompt antisecretory-  
antispasmodic action  
of Quarzan® (clidinium Br)

with the convenience and economy  
of a single medication...  
all advantages in sustaining  
patient compliance



adjunctive  
dual-action

# Librax®

Each capsule contains 5 mg chlordiazepoxide HCl  
and 2.5 mg clidinium Br.

For relief of psychovisceral  
symptoms in irritable bowel  
syndrome\* and duodenal ulcer\*

## A distinctive antianxiety-anticholinergic agent

Please consult complete prescribing information, a summary  
of which follows:

Indications: Based on a review of this drug by the  
National Academy of Sciences—National Research Council  
and/or other information, FDA has classified the indications  
as follows:

"Possibly" effective: as adjunctive therapy in the treat-  
ment of peptic ulcer and in the treatment of the irritable  
bowel syndrome (irritable colon, spastic colon, mucous  
colitis) and acute enterocolitis.  
Final classification of the less-than-effective indications  
requires further investigation.

Contraindications: Patients with glaucoma; prostatic hyper-  
trophy and benign bladder neck obstruction; known hypersen-  
sitivity to chlordiazepoxide hydrochloride and/or clidinium  
bromide.

Warnings: Caution patients about possible combined effects  
with alcohol and other CNS depressants. As with all CNS-acting  
drugs, caution patients against hazardous occupations requiring  
complete mental alertness (e.g., operating machinery, driving).  
Though physical and psychological dependence have rarely  
been reported on recommended doses, use caution in adminis-  
tering Librium® (chlordiazepoxide hydrochloride) to known

addiction-prone individuals or those who might increase dosage;  
withdrawal symptoms (including convulsions), following discon-  
tinuation of the drug and similar to those seen with barbiturates,  
have been reported. Use of any drug in pregnancy, lactation, or  
in women of childbearing age requires that its potential benefits  
be weighed against its possible hazards. As with all anticholiner-  
gic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to small-  
est effective amount to preclude development of ataxia, over-  
sedation or confusion (not more than two capsules per day initially;  
increase gradually as needed and tolerated). Though generally  
not recommended, if combination therapy with other psycho-  
tropics seems indicated, carefully consider pharmacologic effects  
of agents, particularly potentiating drugs such as MAO inhibitors  
and phenothiazines. Observe usual precautions in presence of  
impaired renal or hepatic function. Paradoxical reactions (e.g.,  
excitement, stimulation and acute rage) have been reported in  
psychiatric patients. Employ usual precautions in treatment of  
anxiety states with evidence of impending depression; suicidal  
tendencies may be present and protective measures necessary.  
Variable effects on blood coagulation have been reported very  
rarely in patients receiving the drug and oral anticoagulants.  
Causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not  
seen with either compound alone have been reported with

Librax. When chlordiazepoxide hydrochloride is used alone,  
drowsiness, ataxia and confusion may occur, especially in the  
elderly and debilitated. These are avoidable in most instances by  
proper dosage adjustment, but are also occasionally observed at  
the lower dosage ranges. In a few instances syncope has been  
reported. Also encountered are isolated instances of skin eruptions,  
edema, minor menstrual irregularities, nausea and consti-  
pation, extrapyramidal symptoms, increased and decreased  
libido—all infrequent and generally controlled with dosage re-  
duction; changes in EEG patterns (low-voltage fast activity) may  
appear during and after treatment; blood dyscrasias (including  
agranulocytosis), jaundice and hepatic dysfunction have been  
reported occasionally with chlordiazepoxide hydrochloride, mak-  
ing periodic blood counts and liver function tests advisable dur-  
ing protracted therapy. Adverse effects reported with Librax are  
typical of anticholinergic agents, i.e., dryness of the mouth, blur-  
ring of vision, urinary hesitancy and constipation. Constipation  
has occurred most often when Librax therapy is combined with  
other spasmolytics and/or low residue diets.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

Wednesday, July 7, 1976

MEDICAL TRIBUNE

17



*The Benjamin Rush House, Philadelphia, Pennsylvania*

For The Bicentennial:

## Fund Drive Underway to Restore the Birthplace of Dr. Benjamin Rush



*Benjamin Rush*

SOME MEMBERS of the medical profession are celebrating the Bicentennial by a nation-  
wide fundraising drive to restore the Philadelphia birthplace (above) of Dr. Benjamin  
Rush (1746-1813), "father of American medicine" and one of the six physicians  
who signed the Declaration of Independence (see MT, June 23, 1976). About 40 medi-  
cal and university groups, including the American Psychiatric Association, the Penn-  
sylvania Medical Association, and presidents of the AMA, Princeton University and  
Rutgers College are sponsoring the project. Plans call for reconstruction of the Rush  
birthplace on landscaped grounds at the Philadelphia State Hospital, near the northeast  
gateway to Philadelphia. Dr. Rush founded the College of Physicians, was first professor  
of chemistry at nation's first medical school, the University of Pennsylvania, and pub-  
lished the first book on mental illness in America. Contributions to the restoration fund  
should be sent to Benjamin Rush House Committee, 11 N. 49th St., Philadelphia, Pa.  
19139.



**JOHN HANCOCK'S DEFIANCE.**

John Hancock makes sure King George can read his signature. Looking  
on is Dr. Rush, rear, fourth from left.



The signing of the Declaration of Independence (above) as depicted in  
the famous painting by John Trumbull.

Scottish & Howe  
Sollitt & Co Ltd  
Sutton Healthcare  
Shallcross Pen (UP)  
Smith & Nephew  
Somerville Street  
Sony United King  
St Ivel Ltd B...  
Stratford-Upon-A  
Tate & Lyle Sug  
Taunton Cider  
Telford Foods L  
Tesco Stores L

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John McKee Project Manager  
Vicki Morison Administration Manager  
Isabel Hutchings Conference Manager  
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# Valium® differs from other benzodiazepines (diazepam)

ROCHE

## Valium (diazepam) is the one benzodiazepine with three clinically useful pharmacologic properties

In the research laboratory, Valium demonstrated that it possessed potent psychotherapeutic, muscle relaxant and anticonvulsant properties. But the crucial question remained: would these three properties prove to be clinically useful? Extensive clinical testing gave the answer. Yes. Of all the available benzodiazepines, Valium — and only Valium — has three valuable pharmacologic properties that have all proven to have definite clinical utility. Clearly, this makes Valium one of the most useful agents in a physician's armamentarium.

And, quite likely, one of the most versatile. Today, Valium is indicated in an impressively broad

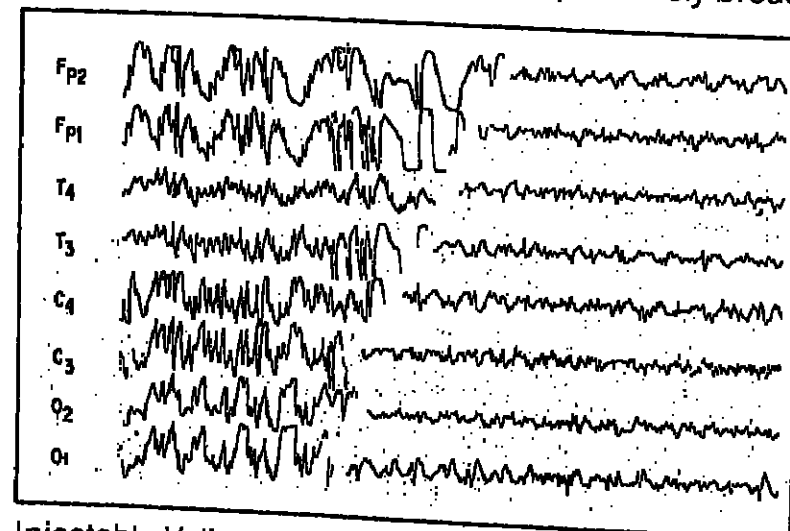
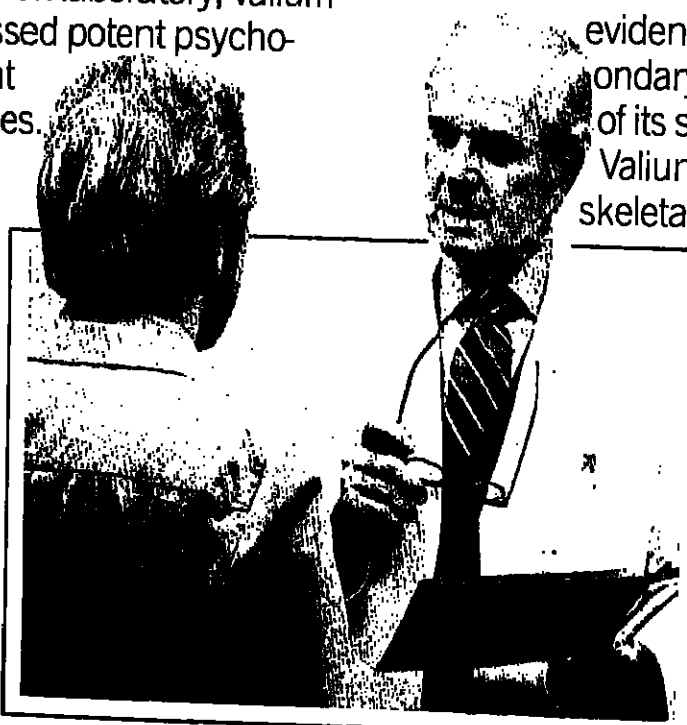
range of disorders. As a psychotherapeutic agent, for instance, it's useful for the relief of undue psychic tension and anxiety whether seen alone or associated with organic and functional disorders. It's also useful in psychoneurotic conditions

evidenced by anxiety with or without secondary depressive symptoms. Because of its skeletal muscle relaxant effect, Valium is a valuable adjunct in relieving skeletal muscle spasm caused by

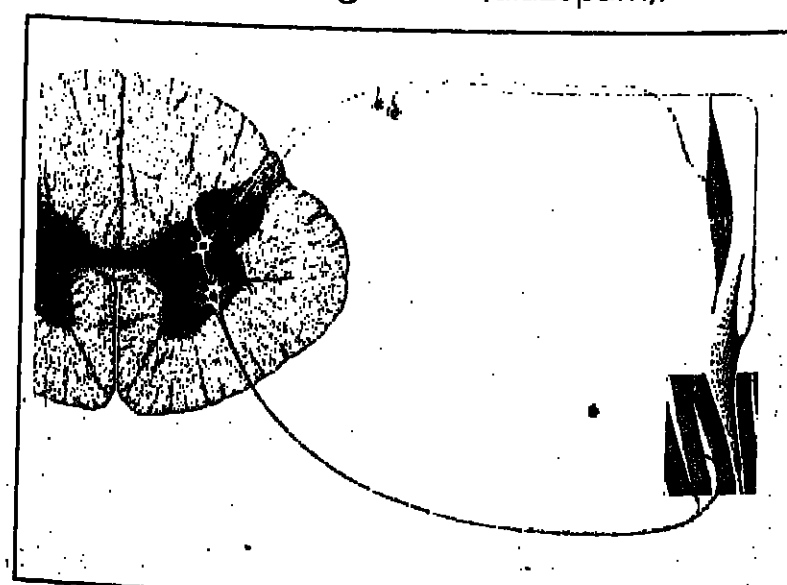
strains, sprains or inflamed skeletal muscles. And its potent anticonvulsant action makes it a preferred drug (given adjunctively I.V.) in status epilepticus.

Drowsiness, ataxia and fatigue are possible side effects, but these and more serious adverse reactions are rarely a problem. Of course, as

with all CNS-acting agents, patients should be cautioned about driving, operating dangerous machines or the simultaneous ingestion of alcohol while taking Valium (diazepam).

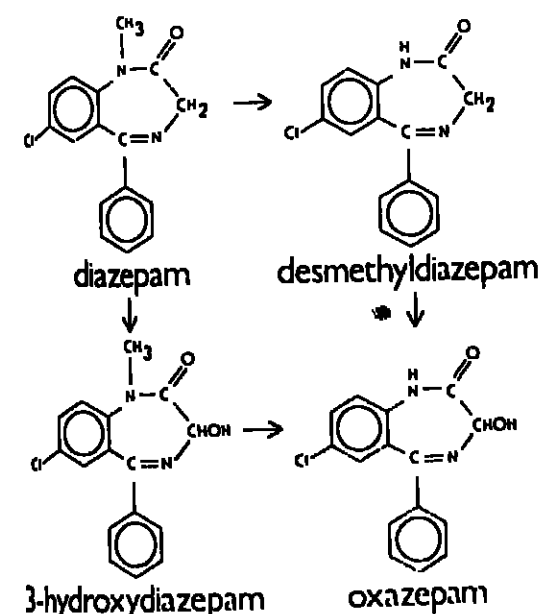


Injectable Valium has distinct anticonvulsant properties. Sample of EEG's in a patient with status epilepticus — before and 15 seconds after Valium 8 mg I.V. Lombroso CT: Neurology 16:629-634, July 1966.



Preliminary studies in both animals and humans have suggested that Valium may also work at the spinal level by enhancing presynaptic inhibition, a mechanism believed to diminish spasm in skeletal muscle.

Only Valium (diazepam) has a pharmacokinetic profile that includes diazepam, active itself, plus other active metabolites



The unique metabolic pathways of Valium (diazepam)

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10-ml vials } 5 mg/ml

Because the various benzodiazepines all have different physical-chemical properties, each, naturally, has a different pharmacokinetic "profile." The "profile" of Valium stands out for a number of reasons. First and foremost is the fact that the major metabolites of Valium, which include desmethyldiazepam, 3-hydroxydiazepam and oxazepam, are all pharmacologically active. And, of course, the parent substance — diazepam itself — is also highly active. Then, too, Valium has demonstrated a highly reliable and consistent pattern of absorption, distribution, metabolism and excretion. Such pharmacokinetic predictability is just one more indication of its overall reliability of performance.

**Valium®  
(diazepam)  
One of a kind.**

Please turn page for a summary of product information.

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**ROCHE** Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

The lack of a correction is exposing the market to still more erratic buffeting at the hands of events. It has clearly

Seven years ago, my family gave me 250 shares of a "junior grade" growth stock in the electronics field. I now have 290 shares, and when the company offered to buy them from me for

You sure did. If you sell it now, you won't miss much. The next rally will be led by the "senior grade" growth stocks.

Send your questions on finance, investments, taxes to Janeway, MEDICAL TRIBUNE, 880 Third Avenue, New York, N.Y. 10022.

"This is probably related to longer service employees who find themselves trapped by service connected benefit plans," Dr. Weiman explained. "It may also be hypothesized that overstimulation is of greater risk potential than understimulation."

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- Readily assimilated
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**Usual Dosage:** ELIXIR—1 to 3 teaspoonsful daily or as directed by physician.  
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**Supplied:** 12 ounce bottles of Elixir; bottles of 100 Tablets.

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**FLX-B12™**  
**Elixir**—each ounce represents: Iron and Ammonium Citrate, 18 gr.; Liver Fraction 1, 3 gr.; Thiamine Hydrochloride, 10 mg; Riboflavin, 4 mg.; Nicotinamide, 20 mg.; Cyanocobalamin (Vit. B12), 20 mcg; Alcohol 8% by volume.  
**Tablets**—each tablet contains: Ferrous Gluconate, 5 gr.; Vitamin C, 60 mg; Cyanocobalamin (Vit. B12), 10 mcg.; Liver Fraction 2, 2 gr.; Thiamine Hydrochloride, 2 mg.; Riboflavin, 2 mg.; Nicotinamide, 20 mcg.

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The studies "strongly suggest the disturbance of the normal metabolism of rhodopsin can, in effect, produce profound disturbance of the normal seeing process," Dr. Wong said. "Disorders of retinal degeneration, symptomatic ophthalmia, macular degeneration and iatrogenically induced blindness from drug toxicities will undoubtedly be clarified in future research efforts."

# THE GOOD DRUGS DO

Confidential deafness: While perceptive



**on average, sleep  
within 17 minutes that  
lasts for 7 to 8 hours  
with fewer nighttime  
awakenings<sup>1</sup>** proved in patients  
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**for patients who need it, continued  
effectiveness over 28 nights<sup>2,3</sup>**

prolonged medication for insomnia is generally not necessary;  
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**proven effectiveness in  
elderly patients with  
verified insomnia<sup>4</sup>**

the greater the degree of insomnia, the greater  
the objective improvement with Dalmane 15 mg  
administered for 7 nights *h.s.*—15 mg is the  
recommended initial dosage for elderly and  
debilitated to help preclude oversedation,  
dizziness or ataxia

**a full night's sleep with a single  
*h.s.* dose<sup>1-8</sup>** patients fall asleep faster, awaken less often  
during the night, sleep longer without repeating dosage

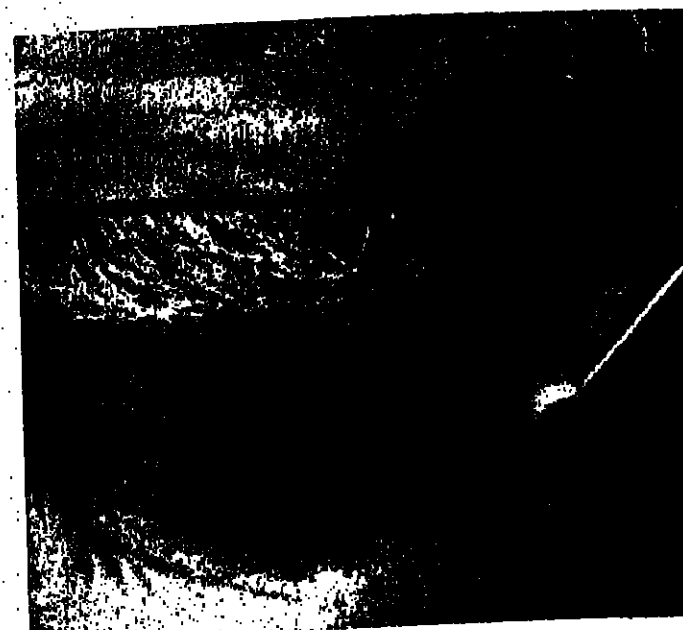
**well tolerated, seldom  
causes morning  
"hang-over"<sup>1</sup>** Dalmane is a

distinctive benzodiazepine specifically indicated for  
sleep with well-documented safety and low  
incidence of morning "hang-over"

**more documentation from the  
sleep research laboratory than  
any other agent for insomnia<sup>1-8</sup>**

polysomnographic techniques provide the most objective  
measurement of effectiveness possible

**relative safety extending  
even to patients on chronic  
warfarin therapy<sup>1,9</sup>** no unacceptable  
fluctuation in prothrombin time has been reported  
with Dalmane



**The  
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Esidrix. It is still unsurpassed as a basic diuretic/antihypertensive.

And many patients with edema rarely need a more potent diuretic.

Contraindications include anuria. Use cautiously in patients with impaired renal or hepatic function.



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(hydrochlorothiazide)  
for year-after-year control  
of mild hypertension

## Esidrix® (hydrochlorothiazide)

**INDICATIONS**  
Hypertension and edema.

**CONTRAINDICATIONS**  
Anuria, hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous.

**WARNINGS**  
Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte imbalance may precipitate hepatic coma.

Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.

Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Use of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

## Nursing Mothers

Thiazides cross the placental barrier and appear in cord blood and breast milk.

**PRECAUTIONS**  
Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremia, hypokalemia, and hypocalcemia). Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs of dehydration, thirst, weakness, lethargy, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbance such as nausea or vomiting.

Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk diuresis; when severe cirrhosis is present, or during concomitant administration of steroids or ACTH. Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digitalis toxicity may exaggerate metabolic effects of hypokalemia, especially with reference to myocardial activity.

Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt, except in rare instances when the hy-

ponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.

Hypuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration.

Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy syndrome. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.

If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.

Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

**ADVERSE REACTIONS**  
**Gastrointestinal**—anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis, Central Nervous System—dizziness, vertigo, paresis, headache, somnolence, dermatologic—hyperuricemia, purpura, photosensitivity, rash, urticaria, necrotizing angitis, Stevens-Johnson syndrome, and other hypersensitivity reactions.

**Hematologic**—leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia. **Cardiovascular**—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. **Other**—hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness. Whenever adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

**DOSEAGE**  
Individualize dosage by titrating for maximum therapeutic response at the lowest possible dose. **Hypertension Initial**—Usual dose 75 mg daily. **Maintenance**—After a weak dosage may be adjusted downward to as little as 25 mg or upward to as much as 100 mg daily. Combined therapy with other antihypertensives may be added gradually and with caution because of the potentiating effect of this drug. Dosages of single-acting blockers should be halved.

**Edema Initial**—25 to 50 mg daily for several days. **Maintenance**—25 to 100 mg daily or intermittently. Refractory patients may require up to 200 mg daily.

**SUPPLIED**  
Tablets, 50 mg (yellow, scored) bottles of 30, 60, 100, 1000, 5000, and Accu-Pak blister units of 100. Tablets, 25 mg (pink, scored) bottles of 30, 60, 100, 1000 and 5000.

Consult complete literature before prescribing. CIBA Pharmaceutical Company, Division of CIBA-GEIGY Corporation, Summit, New Jersey 07901

CIBA

Friday, July 7, 1976

MEDICAL TRIBUNE

29

## Clinical Trials



## Ultrasonic Probe Visualizes Prostate, Bladder Diseases

Medical Tribune Report

Las Vegas—A new transrectal, ultrasonic probe, coupled with a gray scale technique that provides sharper tissue differentiation, appears to show promise in evaluating prostate and bladder cancers, the American Urological Association was told here.

Dr. Martin L. Resnick, Instructor in Urology at the Bowman Gray School of Medicine, said that the new ultrasonic technique should prove to be a useful tool "in helping to increase the detection of early carcinoma that is not readily palpable," in the staging of prostate and bladder carcinoma, in evaluating response to therapy, and even in assessing cervical, uterine, and ovarian diseases.

While ultrasonography has been "a valuable adjunct" in assessing diseases of the brain, kidney, pancreas, and retroperitoneum, Dr. Resnick noted, the prostate and urinary bladder have been inaccessible by this technique because of their positions deep in the pelvis.

Some four years ago, he continued, a transrectal probe was developed that permitted access to these organs. More recently, Dr. Resnick said, a new probe capable of longitudinal and rotational motion has been developed, and this has been coupled with a gray scale converter.

### Unsuspected Ca in Four

In his study, with Drs. James H. Willard and William H. Boyce, prostatic scans were made of 84 patients with clinical findings indicating benign prostatic hyperplasia. The diagnosis was confirmed in 64 of the patients, he said, 52 of whom had prostatectomies. Unsuspected carcinoma was found by sonography in four patients, however, prostatic in eight, and prostatic calculi in four.

In five patients scanned after radical prostatectomy, no recurrence was demonstrated in four, and an unsuspected recurrence was found in one. In 12 patients treated with hormones for ad-

vanced carcinoma, tumor regression was documented in 11, and one was confirmed to be unresponsive. And in seven patients with prostatic nodule, benign hyperplasia was confirmed by sonography in two, carcinoma was found in three, and prostatitis in two, Dr. Resnick said.

Involvement of the seminal vesicles found by sonography in two of the patients with carcinoma was particularly important, Dr. Resnick said, because it indicates the possible role of sonography in staging.

Scans were also carried out in 10 patients with known bladder tumors, Dr. Resnick said, all but one of whom underwent surgical exploration. "Ultrasonography was accurate in detecting tumor invasion through the bladder wall and all Stage C tumors (five patients) were accurately assessed preoperatively."

"All Stage B tumors were also correctly identified, though B1 tumors (three patients) and B2 tumors (two patients) could not be differentiated by this technique." But, he noted, other staging techniques have errors approaching 50% in this category of cancer.

## Medical Meeting Schedule

- Aug. 14 ... American Association of Clinical Chemists, Houston, Tex.
- Aug. 17 ... American Institute of Ultrasound, San Francisco, Calif.
- Aug. 18 ... American Academy of Clinical Toxicology, Seattle, Wash.
- Aug. 18 ... National Medical & Dental Association, Hershey, Pa.
- Aug. 18 ... International Doctors in Alcoholism Anonymous, Los Angeles, Calif.
- Aug. 18 ... National Medical Association, Nashville, Tenn.
- Aug. 18 ... American Society for Clinical Nutrition, East Lansing, Mich.
- Aug. 18 ... South Dakota Black Hills Seminar, Rapid City, S.D.
- Aug. 18 ... Association of Philippine Practicing Physicians in America, Wash., D.C.
- Aug. 18 ... American Society for Pharmacology & Experimental Therapeutics, New Orleans, La.
- Aug. 18 ... American Physiological Society, Philadelphia, Pa.
- Aug. 18 ... International Society for Experimental Hematology, Wash., D.C.
- Aug. 18 ... West Virginia State Medical Association, White Sulphur Springs, W.Va.
- Aug. 18 ... Rocky Mountain Radiological Society, Denver, Colo.
- Aug. 18 ... Tennessee Memorial Cancer Lectures, Memphis, Tenn.
- Aug. 18 ... 4th Internal Congress of IASBMD, Wash., D.C.
- Aug. 18 ... International Congress of the Transplantation Society, New York, N.Y.
- Aug. 18 ... Wyoming State Medical Society, Moran, Wyo.

## IMMATERIA MEDICA

### Candidates' Jokes

Now that everyone knows that Bob Orben writes President Ford's jokes and helps him smooth out their delivery, we're worried about who is going to do Ronald Reagan's material. Reagan's a former actor so he hasn't got delivery problems. His problem lies in the jokes. He's got to top Ford's one-liner: "Ronald Reagan doesn't dye his hair. It's just prematurely orange."

The fellow who invented Senator Claghorn, Fred Allen, is dead, so that leaves him out. But he had a line that maybe Reagan could use. The way it worked was that Senator Claghorn made some ridiculous comment and then said: "That's a joke, son." It made everything funny. But Reagan's attitude is to hardline everything and that leaves little room for fun. *That's a joke, son.*

The Democrats have to worry too.

Bob Orben gave Ford this one for dinners and meetings: "I couldn't find my program so I leaned over to the man sitting next to me and asked, 'What follows Senator Humphrey?' He looked at his watch and said, 'Christmas.'"

Of course, jokes may not help any candidate.

Who wants a funny man in the White House?

### Ach! Das Hangover Kids

We're indebted to a hospital—and deliberately anonymous—librarian in sunny Florida for the following:

"*Stedman's Medical Dictionary*, 22nd edition, has confused me with this entry: Kat' zenjam'mer [Ger. Katzenjammer, headache on morrow of a carousel] Hangover."

"*Stedman* wouldn't go so far as to tell me about the carousel but Webster says it is a merry-go-round, erroneously carousel, and a carousel is a drunken revel, erroneously carousel."

"One of my favorite childhood comic strips was 'The Katzenjammer Kids.' Now I find out the poor little kids were hangover headaches from a drunken revel or from staying on the merry-go-round too long."

"I think I'll stay with the 21st edition. It let them rest in peace."

Best prostatic hyperplasia is shown by ultrasonography. U indicates the urethra and CAP the capsule. Of 84 patients with clinical findings indicating hyperplasia, diagnosis was confirmed in 64 and 52 had prostatectomies.

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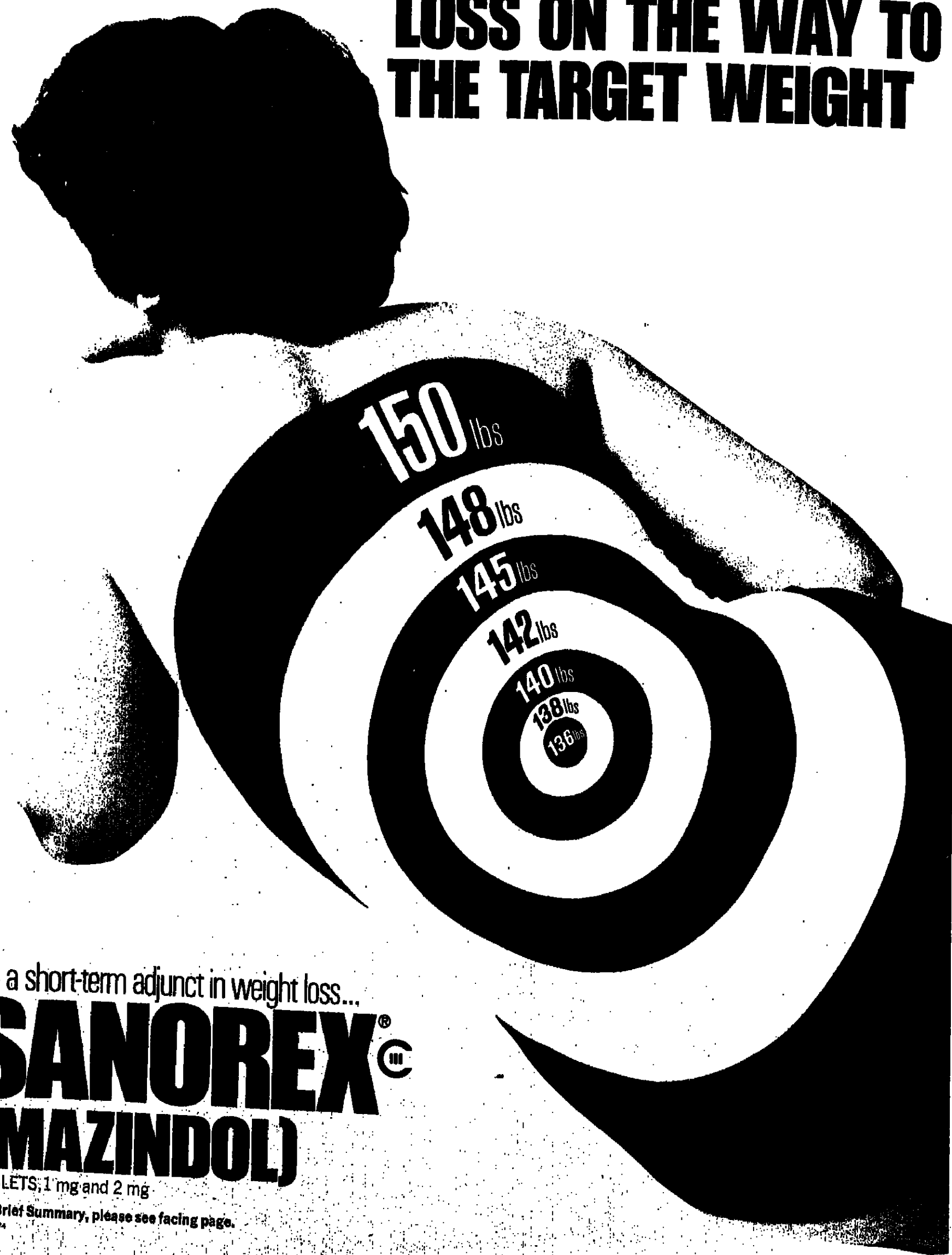
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# CONSISTENT WEIGHT LOSS ON THE WAY TO THE TARGET WEIGHT



As a short-term adjunct in weight loss...

## SANOREX<sup>®</sup> (MAZINDOL)

TABLETS, 1 mg and 2 mg

For Brief Summary, please see facing page.

Wednesday, July 7, 1976

## SANOREX<sup>®</sup> (MAZINDOL)

TABLETS, 1 mg and 2 mg

Indication: In exogenous obesity, as a short-term adjunct in a weight-reduction regimen consisting of caloric restriction. The limited usefulness of this class should be measured against possible risk factors.

Contraindications: Glaucoma; hypersensitivity or idiosyncrasy to the drug; agitated states; history of drug abuse; during, or within 14 days following, administration of monoamine oxidase inhibitors (hypertensive crisis may result).

Warnings: Tolerance to many anorectic drugs may develop within a few weeks; if this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.

Drug Interactions: May decrease the hypotensive effect of guanethidine; patients should be monitored accordingly. May markedly potentiate pressor effect of exogenous catecholamines; if a patient recently taking mazindol must be given a pressor amine agent (e.g., isoproterenol or isoproterenol) for shock (e.g., myocardial infarction), extreme care should be taken in monitoring blood pressure at frequent intervals and initiating pressor therapy with a low initial dose and careful titration.

Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related drugs that have been extensively abused and which produce tolerance and severe psychological dependence. Manifestations of chronic overdosage or withdrawal with mazindol have not been determined in humans. Manifestations have been observed in dogs after the abrupt cessation of prolonged periods of low-dose self-administration of the drug in cages. EEG studies and "kink" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been further defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.

Usage in Pregnancy: An increase in neonatal mortality and a possible increased incidence of rib fractures in rats were observed at relatively high doses.

Usage in Children: Not recommended for use in children under 12 years of age.

Precautions: Insulin requirements in diabetic patients may be altered. Smallest amount of mazindol should be prescribed to prevent overdosage. User should be aware of possibility of overdosage. User should be aware of possibility of overdosage. User should be aware of possibility of overdosage.

Side Effects: Most commonly dry mouth, constipation, nervousness, and insomnia. Cardiovascular: Palpitation, tachycardia, dizziness, insomnia, dysphoria, tremor, depression, drowsiness, weakness, anorexia, dryness of mouth, unpleasant taste, constipation, nausea, other gastric disturbances. Skin: Rash, excessive sweating, alopecia. Endocrine: Impotence, changes in menstrual cycles, reversible on cessation of medication. Other: Reversible on cessation of medication.

Administration: 1 mg three times daily. The lowest effective dose should be used. The lowest effective dose should be used. The lowest effective dose should be used.

There are no data as yet on acute overdosage with mazindol in humans. Signs and symptoms of overdosage with amphetamines and related drugs include restlessness, tremor, rapid heartbeat, fatigue and depression may occur. Fatigue and depression may occur. Fatigue and depression may occur.

For Brief Summary, please see facing page.

MEDICAL TRIBUNE

31

## TRIBUNE SPORTS REPORT

### Slow Marathon Running Favored as Protection from Fatal Coronary Disease

By MICHAEL HERRING  
Medical Tribune Staff

INGELWOOD, CALIF.—The debate over marathon training as protection against heart disease continues to divide experts, but Dr. Thomas Bassler recently told MEDICAL TRIBUNE that he remains convinced that long, slow distance-running, combined with no smoking and an Olympic runner's diet, offers "absolute protection against fatal coronary heart disease."

Dr. Bassler, who is a pathologist at Centinela Hospital here and editor of the American Medical Jogger's Association Newsletter, said the association (about 1,000 doctors who run marathons) has still been unable to document "a single death resulting from coronary heart disease among marathon finishers of any age."

Marathon running, he explained, consists of training until the runner completes 42.3 kilometers (about 26 miles) in a single stretch, followed by maintenance training of six miles a day every other day. The runner's diet is basically macrobiotic, he added, not Spartan, but low in animal fat, salt, hard liquor, wine, and refined foods. "That's what helps you run," Dr. Bassler said he tells patients, knowing that if they eat poorly or start to smoke, they can't keep up the training.

The marathon regimen is not, strictly speaking, protective in itself, but "an index of how well a person is taking care of his heart." However, any nonsmoker who can walk, jog, run, or ski the 26 miles at one time is virtually immune to death from coronary atherosclerosis, Dr. Bassler said.

The latest challenge to Dr. Bassler's assertions (there have been many over the past several years) appears in the June issue of *Annals of Internal Medicine*, which reports a study from Harvard of a 1973 Boston marathoner who collapsed while running and showed



Before running long distances, cardiac patients at Toronto Rehabilitation Center walk indoors, then "graduate" to outdoor jogging as shown.

evidence of myocardial infarction when he died weeks later. However, Dr. Bassler emphasized that the runner collapsed because of heat stroke, which principally affects the brain. He also noted that, while the patient's brain never recovered, his heart (which showed no signs of disease) continued to beat during 50 days of coma. In fact, the autopsy showed the runner had larger-than-normal coronary arteries, he said. "The report is really a case of brain death following heat stroke in weather that knocked 500 runners out of the race."

So far, none of Dr. Bassler's cardiac runners have died of heart disease, despite previous infarcts and poor family history. Furthermore, he believes their coronary arteries "can grow with mileage." Runners who complete 10,000 miles have coronary arteries twice the size of normals, while 20,000-mile runners have arteries three times normal size, he told MEDICAL TRIBUNE.

He also cited Dr. George Mann's 1972 study of Masai warriors, in which 50 hearts from warriors aged 15 to 70 were autopsied. Using careful measurements of arterial lumens, the Vanderbilt study showed an increase in coronary artery size with each ten-year group. Dr. Bassler attributes this to the warriors' training of 12-mile daily treks and noted that, while they do have arteriosclerosis, their enlarged lumens apparently compensate and prevent infarction.

For patients who have smoked in the past, Dr. Bassler recommends a stress test first and strict physician supervision at the beginning of training. "Don't fool around with short races," he also cautioned. Many runners reported to have died of coronary heart disease, he explained, adding that shorter distances may offer current protection, but are not as safe, in the long run, as the long run.

## wine talk

By JOHN CHAMBERS  
Author and Consultant to  
Morrell & Company,  
New York Wine Merchants

### Questions from Readers

I was recently given four bottles of older wines and would appreciate an estimate of their present value. The wines are: Chateau Mouton Rothschild 1929, Chateau Latour 1937, Grandes Echezeaux 1961, and La Tache 1961, both Domaines de la Romanee Conti.

Well-chosen wines increase in value at a fairly consistent rate, roughly doubling their price with each decade. However, since a private individual is forbidden to sell wine, it is a difficult investment to cash in. Nonetheless, by buying early and storing the wine, one does have the pleasure of sharing with friends a beautiful bottle, purchased at modest expense, which would be extremely expensive if purchased at the time of drinking. The value of your wines would be: Chateau Mouton Rothschild 1929: \$150.00-175.00, Chateau Latour 1937: \$75.00, Grandes Echezeaux 1961: \$40.00, and La Tache 1961: \$60.00. The price of the first two would, of course, depend on the condition of the wine and particularly the ullage (i.e. the amount of air space between the cork and the surface of the wine).

I have often heard that California wines are drunk too young. The implication is that they would be much more impressive if properly aged. Is this true, and if so, could you tell me when the following 1970 California Cabernet Sauvignons should be drunk: Mayacamas, Beaulieu Private Reserve, Robert Mondavi Unfiltered?

California wines have enough glycerine (i.e. the viscous quality in a wine which is responsible for smoothness) that most can be drunk young. They do improve, however, and the best of them demand more time to settle the tannin (the dusty, harsh taste in a young wine) and permit the wine to mellow. Of the three you list, the Mondavi can be drunk now, although it will be better in three to five years, the Beaulieu should not be drunk before 1978 (preferably 1980), and the Mayacamas will not be ready until 1985. They are all excellent wines from a top vintage.

Send in any questions you may have about wine. Using the most interesting questions, I will do another QUESTIONS FROM READERS column. However, all questions will be answered whether used in the column or not.

NEXT MONTH: The Present Wine Market—A Time to Buy.

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